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Original article

COMPARISON OF SURGICAL STRESS AND POSTOPERATIVE OUTCOMES BETWEEN OPEN CHOLECYSTECTOMY AND OPEN SUBTOTAL CHOLECYSTECTOMY IN DOGS

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Summary

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Gallbladder disease, particularly gallbladder mucocele, is a common and life-threatening condition in dogs, with high perioperative mortality reported after cholecystectomy. In human medicine, subtotal cholecystectomy has been proposed as an alternative technique to reduce the risk of bile duct injury in cases of severe inflammation. However, this approach has rarely been applied in veterinary surgery. The present experimental study aimed to compare the safety and invasiveness of conventional open cholecystectomy (OC) and open subtotal cholecystectomy (OSC) in healthy dogs. Ten adult Beagles were randomly assigned to either the OC (n=5) or OSC (n=5) group. Postoperative stress and inflammatory responses were evaluated using surgical time, plasma cortisol, C-reactive protein (CRP), white blood cell counts, lymphocyte counts, and serum liver enzymes. Operative time did not differ significantly between the groups. Postoperative cortisol concentrations were significantly lower in the OSC group at 3 and 6 hours, while lymphocyte counts were higher on postoperative days (PODs) 1 and 7 compared with the OC group, indicating reduced surgical stress with OSC. Conversely, CRP was transiently higher in the OSC group on POD 3, likely reflecting local tissue inflammation. No significant differences in liver enzyme or bilirubin levels were observed, and no major complications occurred in either group. These results suggest that OSC can be performed safely and with lower surgical stress than conventional OC, although further studies are warranted to evaluate its clinical application in diseased canine gallbladders.

Key words: cholecystectomy, dog, gallbladder mucocele, subtotal cholecystectomy, surgical stress

INTRODUCTION

Gallbladder diseases in dogs, including gallbladder mucocele, cholecystitis, cholelithiasis, and biliary sludge, are frequently encountered in clinical veterinary practice. Among these, gallbladder mucocele represents a life-threatening extrahepatic biliary disorder, with perioperative mortality reported to reach up to 40% in dogs undergoing cholecystectomy (Rogers *et al.,* 2020). Consequently, early surgical intervention at the asymptomatic stage is recommended (Youn *et al.,* 2018). Concurrent cholecystitis is commonly observed in dogs with gallbladder mucocele (Rogers *et al.,* 2020). Inflammation of the gallbladder wall and surrounding tissues often results in adhesions between the liver and gallbladder, which may complicate the performance of cholecystectomy.

Open cholecystectomy (OC) remains the standard treatment for canine gallbladder disease (Youn *et al.,* 2018; Gondolfe & Hans, 2024). In contrast, approximately 73% of cholecystectomies in human medicine are performed laparoscopically (LC) (Ito *et al.,* 2025). Although LC is minimally invasive and generally preferred by patients, it can be technically challenging in the presence of cholecystitis or unclear pericholecystic anatomy, leading to an increased risk of bile duct injury compared to open surgery (Mangieri *et al.,* 2019; Purzner *et al.,* 2019). Severe inflammation and fibrosis associated with cholecystitis further elevate the risk of bile duct or vascular injury (Purzner *et al.,* 2019). As a result, conversion from LC to OC is not uncommon.

Laparoscopic subtotal cholecystectomy (LSC) has been proposed in human medicine as an alternative to conversion (Roesch-Dietlen *et al.,* 2019; Tay *et al.,* 2020). In LSC, the gallbladder is transected at the neck rather than at the cystic duct, followed by dissection from the hepatic bed. In cases with severe adhesions, part of the gallbladder wall may be incised and left attached to the liver, while the remainder is removed (Shin *et al.,* 2016). Although LSC may be associated with complications such as bile leakage or wound infection, it has been reported as a safe procedure that prevents major complications, including bile duct injury (Roesch-Dietlen *et al.,* 2019).

If a comparable subtotal cholecystectomy approach were applied to dogs via open surgery, it may reduce the mortality associated with severe inflammatory conditions, such as gallbladder mucocele. However, subtotal cholecystectomy is rarely performed in dogs, and its application has not yet been thoroughly investigated in veterinary practice.

Therefore, the present study aimed to compare the safety and postoperative outcomes of open cholecystectomy (OC) and open subtotal cholecystectomy (OSC) in dogs.

MATERIALS AND METHODS

Animals

Ten clinically healthy adult Beagle dogs (1.3±0.1 years old, 10.4±0.4 kg) were utilised in this study. Dogs were randomly assigned to either the OC group (n=5) or the OSC group (n=5). Animals were fed once daily, had *ad libitum* access to water, and were maintained under controlled environmental conditions, including light, temperature, and humidity. All dogs were fasted for 12 hours prior to surgery. All procedures were conducted in accordance with the Kitasato University Laboratory Animal Guidelines and approved by the Kitasato University Laboratory Animal Ethics Committee (No.10-078).

Anaesthesia

Premedication consisted of atropine sulfate (0.025 mg/kg IV; Atropine®, Mitsubishi Tanabe Pharma Corporation, Osaka, Japan), midazolam (0.1 mg/kg IV; Dormicum®, Astellas Pharma Inc., Tokyo, Japan), and fentanyl (5 μg/kg IV; Fentanyl injection solution®, Daiichi Sankyo Propharma, Tokyo, Japan). Anaesthesia was induced with propofol (6 mg/kg IV; Propofol® for Animals, Mylan Seiyaku Co., Ltd., Osaka, Japan) followed by tracheal intubation. Anaesthesia was maintained with isoflurane (Isoflurane® for Animals, Mylan Seiyaku Co., Ltd., Osaka, Japan).

Pain management

In addition to the induction dose of fentanyl, a continuous rate infusion (CRI) of fentanyl (10 μg/kg/h IV) was administered intraoperatively, reduced to 5 μg/kg/h postoperatively, and continued for 6 hours. Meloxicam (0.1 mg/kg SC; Metacam® 0.5% injection, Boehringer Ingelheim Animal Health Japan K.K., Tokyo, Japan) was administered preoperatively and once daily for 3 days postoperatively.

Surgical techniques

- Open cholecystectomy (OC) group

A midline incision was made from 2 cm caudal to the xiphoid process to 2 cm caudal to the umbilicus, and the gallbladder was exposed (Fig. 1A). The gallbladder was retracted using Babcock forceps, and the cystic duct and artery were isolated through surrounding connective tissue using Kelly forceps. A clip applier (Hemoclip Applier®, Teleflex Medical Japan K.K., Tokyo, Japan) was used to place one clip on the gallbladder side and two clips on the common bile duct side for both the cystic duct and artery (Fig. 1B, C). After ligation, the gallbladder was dissected from the hepatic bed using an ultrasonic coagulation incision device (SonoSurg-IU, Olympus Corporation, Tokyo, Japan) (Fig. 1D). The abdominal wall, subcutaneous tissue, and skin were

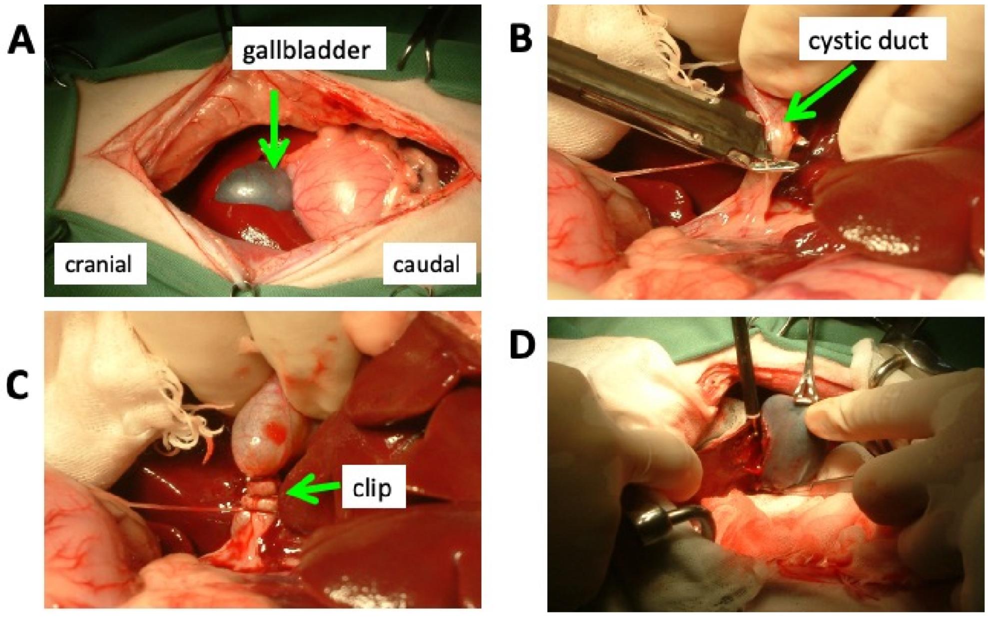


Fig. 1. Open cholecystectomy procedure. A) Gallbladder immediately after laparotomy; B) Ligation of gallbladder duct and gallbladder artery with clip applier; C) Three clips applied; D) Dissection of gallbladder with ultrasonic coagulation incision device.

closed with 3-0 absorbable sutures (PDS II®, Johnson & Johnson, Inc., Tokyo, Japan).

- Open subtotal cholecystectomy (OSC) group

The gallbladder was exposed as in the OC group, and bile was aspirated using a 23G injection needle (Terumo Corporation, Tokyo, Japan). The gallbladder neck was grasped to separate the cystic duct from the cystic artery, and both were clipped in two locations using a clip applier (Fig. 2A). The gallbladder wall was resected, leaving the portion attached to the liver intact (Fig. 2B). The abdominal wall, subcutaneous tissue, and skin were closed with 3-0 absorbable sutures.

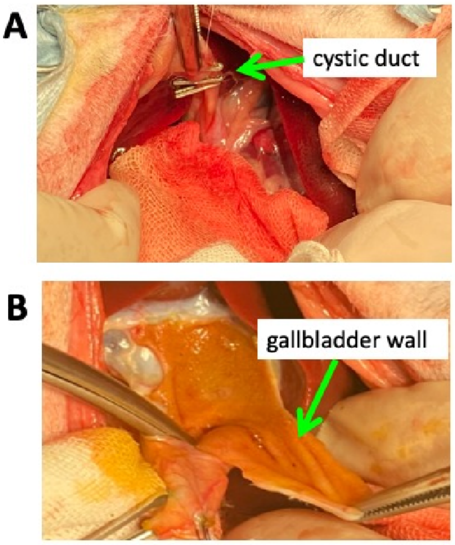


Fig. 2. Open subtotal cholecystectomy procedure. A) Ligation of gallbladder duct and gallbladder artery with clip applier; B) The gallbladder wall was removed using an ultrasonic coagulator, leaving the portion attached to the liver. A look inside the gallbladder wall.

Postoperative management

Feeding was resumed on the day following surgery, and surgical wounds were maintained in a clean condition. Both groups received analgesics as described above for 3 days postoperatively. Additionally, intravenous ampicillin (Viccillin® for injection 1 g, Meiji Seika Pharma Co., Ltd., Tokyo, Japan) was administered at 20 mg/kg twice daily for 7 days postoperatively.

Measurements and sample collection

Blood samples were collected preoperatively (pre), at 1, 3, and 6 hours postoperatively, and on postoperative days (PODs) 1, 3, 5, and 7 from either the flexor cutaneous vein or the lateral saphenous vein. Samples were collected into EDTA, heparin, or serum tubes. Heparinised samples were centrifuged at 3,000 rpm for 5 minutes at 4 °C, and plasma was stored at –20 °C until analysis. Serum samples were centrifuged at 3,000 rpm for 10 minutes at 4 °C and stored under identical conditions until analysis.

Surgical time. Operative time was defined as the interval from skin incision to completion of skin closure.

C-reactive protein (CRP). CRP concentrations were measured using a canine CRP immunoturbidimetric assay (LaserCRP-2, Arrows Corporation, Osaka, Japan) according to the manufacturer's instructions. Measurements were obtained preoperatively, at 1, 3, and 6 hours postoperatively, and on PODs 1, 3, 5, and 7.

Cortisol concentration. Plasma cortisol concentrations were measured by an external clinical laboratory (SRL Corporation, Tokyo, Japan) using the electrochemiluminescence immunoassay (ECLIA) method at the same time points as CRP.

Total white blood cell (WBC) and lymphocyte counts. Total WBC counts were determined preoperatively and on PODs 1, 3, 5, and 7 using an automated haematology analyzer (MEK-6558 Celltac α, Nihon Kohden Corporation, Tokyo, Japan). Lymphocyte counts were calculated from leukocyte differentials obtained from peripheral blood smear evaluations.

Plasma ALT, ALP, and total bilirubin (TB). Plasma concentrations of alanine aminotransferase (ALT), alkaline phosphatase (ALP), and total bilirubin (TB) were measured preoperatively and on PODs 1, 3, 5, and 7 using an automated biochemical analyzer (Siemens Dimension RXL MAX, Siemens Japan K.K., Tokyo, Japan).

Statistical analysis

Data are expressed as mean ± standard deviation (SD). Statistical comparisons between groups were performed using Student's *t*-test. Differences were considered statistically significant at $P<0.05$.

RESULTS

There was no significant difference in operative time between the OC and OSC groups (Fig. 3).

CRP was significantly lower in the OC group than in the OSC group on postoperative day 3 ($P<0.05$) (Fig. 4A). Cortisol levels were significantly lower in the OSC group than in the OC group at 3 and 6 hours postoperatively ($P<0.05$) (Fig. 4B).

Total white blood cell counts were not significantly different between the OC and OSC groups (Fig. 5A). Lymphocyte counts were significantly lower in the OC group than in the OSC group on postoperative days 1 and 7 ($P<0.05$) (Fig. 5B).

Blood plasma ALT, ALP, and TB did not differ significantly between the OC and OSC groups (Fig. 6).

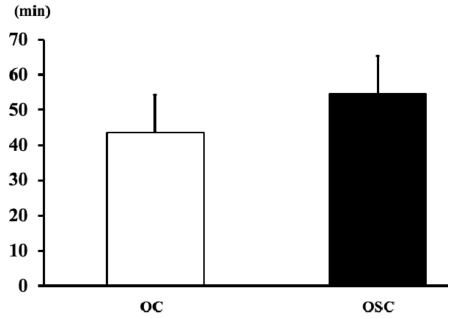


Fig. 3. Comparison of surgical time (mean ± SD; n=5) between open cholecystectomy (OC) and open subtotal cholecystectomy (OSC) groups.

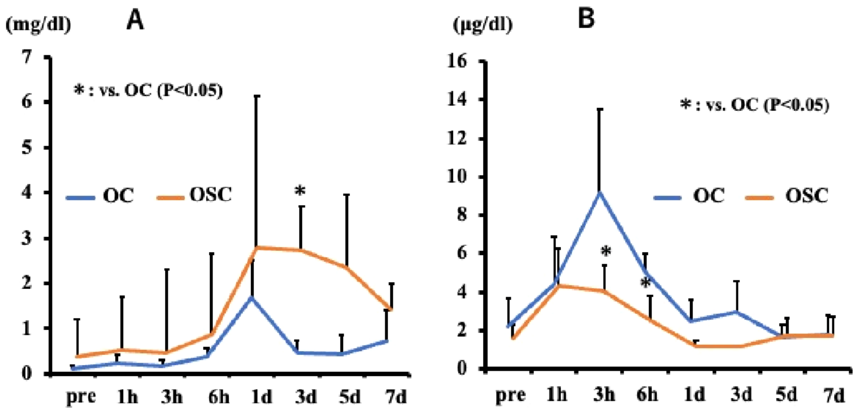


Fig. 4. Comparison of CRP (A) and cortisol (B) levels in the open cholecystectomy (OC) and open subtotal cholecystectomy (OSC) groups. Data are presented as mean ± SD (n=5).

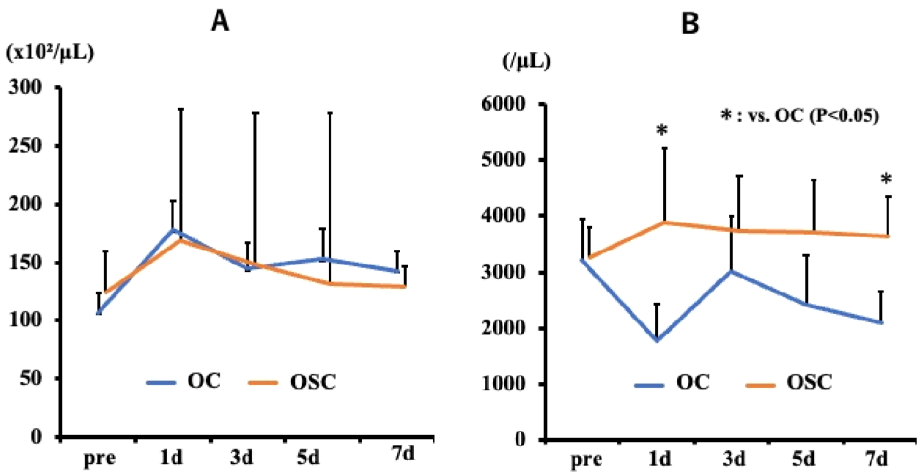
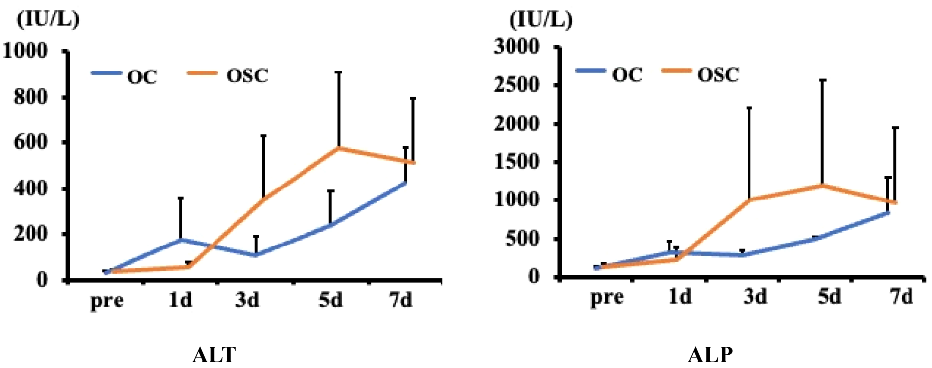


Fig. 5. Comparison of total white blood cell (A) and lymphocyte counts (B) in the open cholecystectomy (OC) and open subtotal cholecystectomy (OSC) groups. Data are presented as mean ± SD (n=5).



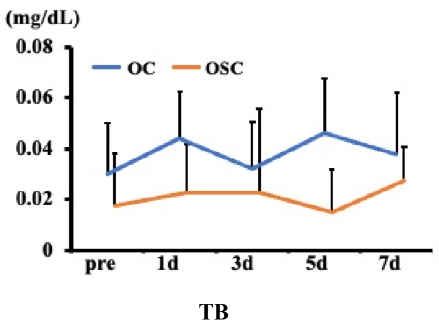


Fig. 6. Comparison of alanine aminotransferase (ALT), alkaline phosphatase (ALP), and total bilirubin (TB) in the open cholecystectomy (OC) and open subtotal cholecystectomy (OSC) groups. Data are presented as mean ± SD (n=5).

DISCUSSION

In this study, cortisol concentrations, total leukocyte counts, lymphocyte counts, and C-reactive protein (CRP) levels were evaluated to compare the invasiveness of conventional cholecystectomy (OC) and open subtotal cholecystectomy (OSC). Cortisol secretion from the adrenal cortex is rapidly elevated following surgical stimulation via adrenocorticotropic hormone (ACTH) and is widely recognised as an indicator of surgical stress (Matovic & Delibegovic, 2019). In dogs, as in humans, surgical stress has been reported to increase plasma cortisol levels and decrease lymphocyte counts (Yamada *et al.,* 2002). In the present study, dogs undergoing OC exhibited higher postoperative cortisol levels and lower lymphocyte counts compared with those undergoing OSC. Although total leukocyte counts tended to increase postoperatively in the OC group, the differences were not statistically significant. These findings suggest that OSC induces a lower degree of surgical stress than conventional OC.

Conversely, CRP levels were higher in the OSC group than in the OC group. Potential explanations include hepatic tissue injury resulting from the use of the ultrasonic coagulation and cutting device during gallbladder wall transection, as well as local inflammatory responses due to bile leakage (Aikawa *et al.,* 2022). However, CRP levels peaked transiently and subsequently decreased without clinical sequelae.

As healthy dogs were used in this experiment, dissection of Calot's triangle and gallbladder wall in the OC group was relatively straightforward compared with cases of cholecystitis. Therefore, the deliberate transection of the gallbladder wall in the OSC group may have contributed to temporarily greater inflammatory responses than in the OC group. No significant differences in plasma ALT, ALP, or total bilirubin (TB) were observed between the groups, although transient postoperative elevations in ALT and ALP occurred in both groups. In human patients, postoperative elevations in liver enzymes are commonly observed after laparoscopic cholecystectomy and are not associated with adverse clinical outcomes (Maleknia & Ebrahimi, 2020).

Major complications associated with OC include bile duct injury and haemorrhage from the hepatic bed or pericholecystic vessels, and it is crucial to balance the benefits of complete gallbladder removal with these risks. In humans, acute cholecystitis is the primary indication for cholecystectomy, whereas in dogs, gallbladder mucocele is the predominant indication, with the incidence of concurrent cholecystitis reported at 28.8% (Rogers, 2020). When the potential complications of total gallbladder removal are anticipated to be more severe than those associated with partial removal, OSC may represent a viable alternative. Subtotal cholecystectomy can prevent major bleeding from the hepatic bed and reduce the risk of bile duct injury, although minor bile leakage and inflammation of the residual gallbladder wall remain concerns. In the present study, minor intra-abdominal bile leakage occurred during gallbladder wall transection, but no OSC-related complications were observed. In one OSC dog, the residual gallbladder wall was re-examined seven days postoperatively (Fig. 7), revealing no bile leakage, wall inflammation, or adhesion to the liver.

Human studies indicate that although bile leakage is more frequent after subtotal cholecystectomy, it is generally a minor complication (Roesch-Dietlen *et al.,* 2019). While retention of the gallbladder wall in cases of severe cholecystitis may

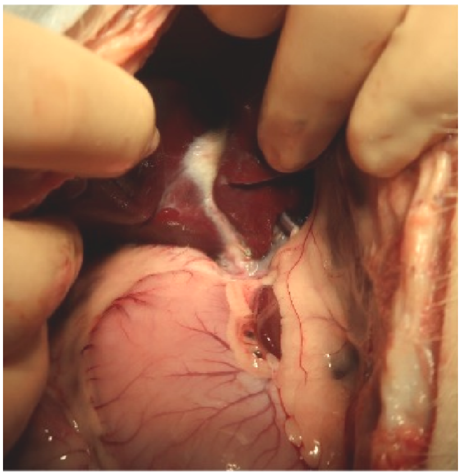


Fig. 7. A dog in the open subtotal cholecystectomy (OSC) group one week after subtotal cholecystectomy. No adhesions to surrounding tissues were observed.

theoretically increase the risk of infection, the incidence of surgical site infection and intra-abdominal abscess formation does not appear to be influenced by the residual gallbladder wall (Shin *et al.,* 2016). Moreover, bile cultures are typically negative in most canine gallbladder mucocele cases (Crews *et al.,* 2009), suggesting a low likelihood of infection originating from the residual wall. In humans, bile leakage following subtotal cholecystectomy can be managed via endoscopic stent placement, and intraoperative drain placement is recommended when the gallbladder neck is left dissected and open (Purzner *et al.,* 2019). Although no bile leakage was observed in the present study, the necessity of such interventions in dogs warrants further investigation. In addition, for cases with common bile duct obstruction, it is necessary to relieve the obstruction through procedures such as lavage.

This study is limited by the use of healthy dogs and the absence of long-term postoperative follow-up. Further studies are required to determine the clinical feasibility of OSC in veterinary patients, particularly with respect to complication rates in diseased gallbladders.

CONCLUSIONS

Open subtotal cholecystectomy was performed without major perioperative complications and was associated with lower surgical stress compared with conventional open cholecystectomy. Although CRP levels were transiently elevated following OSC, no clinical complications were observed. These findings suggest that OSC may represent a safe and effective surgical option in dogs, particularly in cases of severe cholecystitis or when the risk of bile duct injury is elevated. Further clinical studies are warranted to assess long-term outcomes and complication rates in affected canine patients.

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