Glisson's capsule cauterisation is associated with increased postoperative pain after laparoscopic cholecystectomy: a prospective case-control study

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ABSTRACT

INTRODUCTION Postoperative pain after laparoscopic cholecystectomy has three components: parietal, visceral and referred pain felt at the shoulder. Visceral peritoneal injury on the liver (Glisson's capsule) during cauterisation sometimes occurs as an unavoidable complication of the operation. Its effect on postoperative pain has not been quantified. In this study, we aimed to evaluate the association between Glisson's capsule injury and postoperative pain following laparoscopic cholecystectomy.

METHODS The study was a prospective case-control of planned standard laparoscopic cholecystectomy with standardized anaesthesia protocol in patients with benign gallbladder disease. Visual analogue scale (VAS) abdominal pain scores were noted at 2 and 24 hours after the operation. One surgical team performed the operations. Operative videos were recorded and examined later by another team to detect presence of Glisson's capsule cauterisation. Eighty-one patients were enrolled into the study. After examination of the operative videos, 46 patients with visceral peritoneal injury were included in the study group, and the remaining 35 formed the control group.

RESULTS VAS pain score at postoperative 2 and 24 hours was significantly higher in the study group than control ($P = 0.027$ and 0.017 , respectively).

CONCLUSIONS Glisson's capsule cauterisation in laparoscopic cholecystectomy is associated with increased postoperative pain. Additional efforts are recommended to prevent unintentional cauterisation.

KEYWORDS

Laparoscopic cholecystectomy – Postoperative pain – Glisson's capsule injury – Visceral peritoneal injury

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Introduction

Laparoscopic cholecystectomy is one of the most commonly performed abdominal surgical procedures, and is considered the 'gold standard' for the surgical treatment of gallstone disease.^{1,2} The advantages of the procedure are milder postoperative pain, reduced analgesia and shorter recovery period and hospital stay, compared with a traditional open procedure.^{3–5}

The pain that occurs after laparoscopic cholecystectomy can be divided into three types: visceral, parietal and shoulder pain. Visceral pain usually occurs due to the surgical dissection and tissue stretch by handling at the gallbladder bed. This type of pain is felt by the innervation of the visceral peritoneum covering the majority of the abdominal viscera via the same nerve supply as the neighbouring viscera. Parietal or somatic pain is caused by the trauma to the abdominal wall by the insertion of the trocars. Shoulder pain

is frequent in the postoperative period, and is thought to be related to residual carbon dioxide.^{6,7}

Studies of pain mechanisms are usually based on somatic rather than visceral nociception. However, more complications are associated with accessing visceral structures, with adequate visceral stimuli studied in research models. Nociceptive mechanisms in both pain stimuli have common features and but differ in neurology and psychology. Treatment of both forms of pain is largely independent of the accompanying disease. The pain itself is thus regarded as a syndrome rather than a symptom or by-product of illness.⁸

During dissection of the gallbladder, the liver capsule (the visceral peritoneum of the liver, Glisson's capsule) may be cauterised unintentionally if a cautery instrument slips or necessarily during manipulation due to a difficult dissection. The possible relation between visceral peritoneal injury and postoperative pain has not been studied rigorously. The aim of this study was to evaluate the association between visceral

peritoneal (Glisson's capsule) injury due to cauterisation during laparoscopic cholecystectomy and postoperative pain.

Materials and Methods

We designed a prospective case-control study. The institutional review board approved the study and the universal principles of the 1964 Declaration of Helsinki and its later amendments were applied. Written informed consent was obtained from all patients.

Participants

Patients scheduled for laparoscopic cholecystectomy with presumptive diagnosis of benign gallbladder disease (i.e., gallstone, gallbladder polyp and American Society of Anesthesiologists physical status I-II) were assessed. A total of 116 patients were assessed for eligibility for the study; 12 refused to participate in the study and 7 were excluded for concurrent chronic diseases such as osteoporosis, liver, pulmonary or renal insufficiencies or malignancy. After exclusion of these patients, 97 were scheduled for laparoscopic cholecystectomy; 16 were then excluded from the study due to operative findings of acute cholecystitis ($n = 5$), operation time over 90 minutes ($n = 4$), conversion to open surgery ($n = 4$), surgery requiring placement of drains ($n = 3$) and the remaining 81 patients were enrolled. After analysis of the operative videos (group allocation), 46 patients (56.8%) with cauterisation were allocated to the study group, and the remaining 35 (43.2%) constituted the control group. Patient characteristics and operative data are provided in Table 1.

The visual analogue scale (VAS), graded from 0 (no pain) to 10 (the worst imaginable pain), was explained to patients before the operation.

Anaesthesia

The patients were premedicated with 10mg diazepam orally approximately 1 hour before anaesthesia. All patients received a standardized anaesthesia protocol, which included standard monitoring (electrocardiography, noninvasive blood pressure, pulse oximetry and CO₂ analysis).

Operative management

Standard laparoscopic cholecystectomy was performed by using four trocars (two 5mm, two 10mm) and creation of CO₂ pneumoperitoneum at 12mmHg pressure was justified in all patients. First entry and insufflation were performed by Veress needle, which was inserted by positioning the fascia upwards with a Kocher clamp after transverse incision just under the umbilicus. All the operations were performed by one surgical team (FB, AS) who were experienced in laparoscopic surgery. Umbilical trocar sites of patients were closed with one polyglactin suture. Operative data are shown in Table 1.

Postoperative analgesia

A standardized postoperative analgesia regimen was used, consisting of metamizol sodium 1mg intravenously (IV) after induction of anaesthesia and repeated after surgery at every 6 hours for the first 24 hours. Paracetamol 500mg orally, initiated 30 minutes before the surgery and repeated after surgery every 6 hours for the first 24 hours. Titrated IV doses of tramadol were administered as rescue opioid analgesia if the VAS pain score was greater than 4 or inadequate pain relief with standard analgesia was indicated by the patient.

Data collection

Demographic data including age, gender, weight in kilograms and height in metres were recorded preoperatively. Body mass index was calculated as weight in kilograms divided by the square of height in metres (kg/m²).

Operation were recorded on video during surgery and watched postoperatively by two general surgeons (MH, YO) who did not attend the operation. Glisson's capsule cauterisation in one of the study patients is showed in Fig 1. Any damage from cauterisation over the Glisson's capsule of the liver far from dissection area of the gallbladder with size of longer than 3mm (decided with the length of tip of 5mm laparoscopic dissector measured as 3mm) was defined as 'cauterised'. Patients were divided into two groups according to their cauterisation status; the study group included 'cauterised' patients. The remaining patients constituted the control group. Primary outcome variables were VAS abdominal pain scores at 2 and 24 hours postoperatively, and amount of

Table 1 Patient characteristics

Characteristic	Study group ($n = 46$)	Control group ($n = 35$)	P value
Age, mean $\pm$ SD	46.4 $\pm$ 14.4	48.6 $\pm$ 15.2	0.515 ^a
Gender: male/female	11/35	6/29	0.585 ^b
Height, mean $\pm$ SD	164 $\pm$ 7.2	164 $\pm$ 6.1	0.601 ^a
Weight, mean $\pm$ SD	80.8 $\pm$ 16.9	75.6 $\pm$ 14.4	0.143 ^a
BMI, median (IQR)	28.2 (25.4–33.3)	26.8 (24.2–33.2)	0.149 ^c
Operative time, minute, median (IQR)	76.5 (58.8–88.5)	76 (61–89)	0.6 ^c

^at-test; ^bFisher exact test, ^cMann-Whitney test
BMI, body mass index; IQR, interquartile range; SD, standard deviation

Figure 1 Intraoperative view of cauterised Glisson's capsule (arrow: cauterised area).

opioid analgesia administered. In the absence of any complications, patients were discharged 24 hours postoperatively after the completion of the 24-hour VAS score.

Sample size

We used the transversus abdominis plane block study of Petersen et al.⁹ to calculate sample size. We estimated that, with a sample size of 80 patients, the study would have 90% power to show a 40% difference in the rate of the primary outcome, with a double-sided type I error rate of 5–10%. An additional 35 patients were recruited to overcome dropout, refusal and exclusion. The study was completed with 81 patients.

Statistical analysis

Statistical analysis was performed using the SPSS version 22.0 and PASS 2008 statistical software. Normal distributions of the variables were assessed via the Kolmogorov–Smirnov test and histograms. Normally distributed continuous variables were expressed as mean plus or minus standard deviation and median and interquartile ranges were used for non-normally distributed continuous variables. Categorical variables were expressed as frequencies and percentages. Baseline characteristics of the study and control groups were

compared using the t-test for normally distributed continuous variables and Mann-Whitney U test for continuous variables without normal distribution and ordinal variables. Fisher's exact test was used to compare categorical variables. The statistical results were presented at a 95% confidence interval. The differences were considered statistically significant if the *P* value was less than 0.05.

Results

The main finding of this study was that cauterisation of Glisson's capsule of the liver during laparoscopic cholecystectomy was found to be associated with increased postoperative pain and increased opioid analgesia. Demographic findings such as age and gender showed no difference between the groups ($P = 0.515$ and $P = 0.585$, respectively). There was no difference between the groups with respect to patients' height, weight, body mass index and operating time ($P > 0.05$ for all). However, VAS pain scores at 2 and 24 hours postoperatively were significantly higher in the study group than in the control group ($P = 0.027$ and $P = 0.017$, respectively; Table 2, Fig 2). Opioid consumption was recorded in 27 (58.7%) patients in the study and 10 (28.6%) in the control group. There were significantly more patients requiring opioid in study group ($P = 0.013$). All patients were discharged on the first postoperative day with no complications.

Discussion

The gallbladder is a pear-shaped organ lying below liver segments IVB and V. It has an inferior peritoneal surface that is closely in contact with the gallbladder bed in the liver. However, the cystic plate, a condensation of fibroareolar tissue, separates the gallbladder from the liver parenchyma and is not referred as an extension from peritoneum.¹⁰ Glisson's capsule, the equivalent of the visceral peritoneum of the liver, is a layer of connective tissue surrounding the liver. It covers the hepatic artery, portal vein and bile ducts within the liver and causes the sense of pain in the upper right quadrant.^{10,11} In this study, cauterisation of Glisson's capsule of the liver during the dissection of the gallbladder was defined as an injury to the visceral peritoneum.

Our hypothesis was that any trauma to the visceral peritoneum, such as a burn due to cauterisation, may increase postoperative pain. We found that the abdominal pain scores

Table 2 Analysis of the groups based on visual analogue scale (VAS) score and rescue analgesia use

	Study group (<i>n</i> = 46)	Control group (<i>n</i> = 35)	<i>P</i> value
Postoperative VAS:			
2 hours, median (IQR)	3 (2–5)	3 (2–3)	0.027 ^a
24 hours, median (IQR)	2 (2–4)	2 (2–2)	0.017 ^a
Rescue analgesia (opioid) use <i>n</i> (%)	27 (58.7)	10 (28.6)	0.013 ^b

^a Mann-Whitney test, ^b Fisher exact test; IQR, Inter quartile range

as calculated from the VAS were significantly higher in patients with cauterisation of Glisson's capsule of the liver during laparoscopic cholecystectomy, and the VAS scores at 2 hours postoperatively were higher than at 24 hours postoperatively. As the cystic plate has no peritoneal connection, we did not count cauterisation causing injury within the cystic plate. Dissection of the gallbladder from the liver bed was performed by the same standard surgical team and method.

In some studies, it has been mentioned that visceral pain accounts for most of the pain in the early postoperative period.⁸ Other studies have stated that the largest component in abdominal pain is formed by the parietal peritoneum, which is derived from the incision site, followed by pneumoperitoneum and surgical procedures such as cholecystectomy.^{7,12} Pain caused by the surgical incision has been thought to be the most important component and has been shown to be more intense than visceral pain during the first 48 hours after laparoscopic cholecystectomy.¹⁵ Although some studies have shown that injection of a local anaesthetic agent to trocar entry sites does help pain relief, other studies did not attempt to show a positive association with regard to pain relief and have suggested that parietal pain does not contribute substantially to the total pain.^{7,14,15} The origin of postoperative pain thus remains controversial.

Post-laparoscopy pain has multifactorial aetiology, including visceral pain from dissected peritoneum surrounding the gallbladder, somatic pain from retained intraperitoneal blood or bile, insufflation of carbon dioxide with distension of the parietal peritoneum, and traumatic injury related to the trocars.^{16,17} Treatment of each contributing factor in an isolated manner may therefore not achieve the desired result. However, there is increasing evidence that ageing and gender may have some impact on the development and progression of visceral pathology and pain. It has been reported that visceral pain syndromes are less intense in adults of advanced age than in younger individuals.^{17–19} As visceral pain arises as a diffuse and poorly defined sensation caused by the activation of nociceptors of the thoracic, pelvic

or abdominal viscera (organs), it is thought that visceral pain is perceived more diffusely than noxious cutaneous stimulation with respect to location and timing.^{20,21} This issue can be regarded as an important factor for the evaluation of the severity of the postoperative pain.

This study demonstrates that cauterisation of Glisson's capsule of the liver increases postoperative pain and need for opioid analgesia after laparoscopic cholecystectomy. The study has a number of possible limitations. Other contributing factors, such as a difference in cauterisation of the liver parenchyma, may be involved. If such other contributing factors are regarded as the same for all patients, it may be concluded that the difference in the postoperative VAS score and need for opioid usage originate from the cauterisation of Glisson's capsule of the liver. Nevertheless, the surgeon is in a unique position to influence many factors by minor changes in technique, with a corresponding additive improvement in the outcome.^{6,22} In the light of the findings of this study, it is recommended that surgeons should endeavour to prevent unnecessary liver cauterisation.

In our study, rationale for the exclusion criteria was that they might affect the development and severity of postoperative pain. Acute cholecystitis might affect postoperative pain because of intense inflammation. Operative time over 90 minutes might also affect postoperative pain by increasing anaesthesia time and drug usage; therefore, we used these criteria for exclusion.

The main limitations of the study were the challenges in the selection or standardization of cauterised patients. The condition, Glisson's capsule cauterisation, was unintentional and the length of the cauterised area will differ between patients. Although finding a standard expression of the length of the cauterised area may be challenging, the effect on the pain may not be different between the cauterised patients. For this reason, we did not use a scale for size of this area; instead, we designated patients as cauterised or not.

Conclusion

Cauterisation of Glisson's capsule of the liver during laparoscopic cholecystectomy has a negative effect on postoperative pain. The utmost attention should be paid to positioning the gallbladder away from the liver during dissection to prevent damage by cauterisation during the operation, if possible.

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