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Harmonic Scalpel versus Monopolar Electrocauterization in Cholecystectomy

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ABSTRACT

Background and Objectives: Laparoscopic cholecystectomy (LC) using surgical electrocautery is considered to be the gold standard procedure for the treatment of uncomplicated cholecystitis and cholelithiasis. The objective of the current study was to evaluate the effectiveness and safety of the Harmonic scalpel, an advanced laparoscopic technique associated with less thermal damage in LC, when compared to electrocautery.

Methods: From October 2010 through June 2013, a total of 198 patients were randomly allocated to LC with a Harmonic scalpel (experimental group, 117 patients) or conventional monopolar electrocautery (control group, 81 patients). The main outcome measures were operative time, blood loss, conversion to laparotomy, postoperative hospital stay, post-LC pain, and cost effectiveness.

Results: The 2 groups were comparable with respect to baseline patient characteristics. When compared to conventional monopolar electrocautery, there were no significant reductions in the operative time, bleeding, frequency of conversion to laparotomy, and duration of postoperative recovery with the Harmonic scalpel ($P > .05$ for all).

Conclusions: Laparoscopic cholecystectomy using conventional monopolar electrocautery is as effective and safe as that with the Harmonic scalpel, for treating uncomplicated cholecystitis and cholelithiasis.

Key words: Electrocautery, Laparoscopic cholecystectomy, Harmonic scalpel

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INTRODUCTION

Laparoscopic cholecystectomy (LC) has been replacing conventional open cholecystectomy as the gold standard treatment modality for uncomplicated acute or chronic cholecystitis and cholelithiasis. The reason may be its well-recognized minimal invasiveness and expedited postoperative recovery.[1] The standard LC is normally performed with a monopolar electrocautery, usually an electrosurgical hook, especially for the dissection and coagulation of the gall bladder, cholecystic duct, and the cholecystic artery.[2] However, use of electrocautery in LC may cause excessive surgical smoke from cauterizing the tissues and may compromise the precision of dissection.[3] Furthermore, electrocauterization may cause iatrogenic injury of adjacent vessels and solid organs, such as the common bile duct[4] and the small intestine[5] *via* thermal side effects.

The Harmonic scalpel (Ethicon EndoSurgery Inc., Johnson & Johnson Medical SpA, Somerville, NJ, USA) is an advanced, minimally invasive surgical device that has been used in LC for approximately a decade.[6] The scalpel enables synchronous cutting, coagulation, and cavitation of the thicker tissue by a high-frequency (55,500 Hz) vibration, which generates heat by tissue stress and friction to degenerate tissue protein.[7] This technique transfers minimal energy to the tissues in proximity and thereby minimizes the risk of collateral thermal damage.[7] In addition, using a Harmonic scalpel can securely close and seal the biliary ducts and vessels with a diameter of ≤5 mm without requiring vessel clipping.[8]

Results of studies have suggested either statistically significant or clinically limited advantages of using the Harmonic scalpel over electrocauterization.[9–12] The primary objective of this study was to evaluate the effectiveness and the safety of Harmonic scalpel, an advanced laparoscopic technique associated with less thermal damage in LC when compared to electrocautery.

MATERIALS AND METHODS

Study Design

This study was an open-label, assessor-blinded, randomized, controlled trial conducted at a single academic ter-

tiary care institute. The investigators and patients were not blinded. The study protocol was approved by the Institutional Review Board (IRB) at Foshan Municipal Hospital, affiliated with Southern Medical University, in accordance with the latest version of the Declaration of Helsinki, the International Conference on Harmonization Guidelines for Good Clinical Practice, as well as the national legislation of the Chinese Food and Drug Administration. From October 2010 through June 2013, a total of 287 patients were prospectively and consecutively hospitalized for emergency or elective LC and screened for eligibility for this study. Of these patients, 198 were found to be eligible for this study. All the patients voluntarily gave written informed consent, before participating in this study. All eligible patients were equally and randomly assigned to LC, with open-label Harmonic scalpel (the experimental group, 117 patients) or conventional monopolar electrocautery (the control group, 81 patients). The patients were equally and randomly assigned with the help of a computer-generated random number table at a block size of 6 blinded to the investigators and the patients. The randomization was not stratified but centrally managed and concealed at the time of inclusion; a sealed envelope describing the patient allocation was drawn and opened by an independent research nurse on admission to the operating room. All LC procedures were performed by an assigned surgical team, including resident surgeons, anesthesiologists, radiologists, clinical pathologists, surgical nurses, and full-time research staff, led by 2 board-certified laparoscopic surgeons with a previous total case volume of more than 1000 conventional LC procedures and ~300 LC procedures with the Harmonic scalpel.

Inclusion and Exclusion Criteria

All patients were screened for eligibility for enrollment. The preoperative assessment included a history taken by interview and medical chart review, physical examination, routine hematology assessment, clinical biochemistry, virologic serology, electrocardiography, chest X-ray, and upper abdominal ultrasonography. The inclusion criteria were as follows: aged 20–70 years; physical status class I or II, according to American Society of Anesthesiologists (ASA); diagnosis of simple acute or chronic cholecystitis, cholelithiasis, or gallbladder polypoid lesion on abdominal ultrasound or computed tomography (CT) scan; and suitability for LC because of the presence of clinically significant symptoms, oversized gallstones, or prophylaxis of malignancy in high-risk patients. The exclusion criteria were as follows: age <20 years or >70 years; pregnant or lactating women; pre-existing morbid obesity (body mass index [BMI, measure of weight in kilograms divided by the height in meters squared] >40 kg/m^2); ASA class III or IV; complicated intrahepatic or extrahepatic bile duct stones; complicated acute pancreatitis; suspected gallbladder malignancy; history of previous upper abdominal open surgery; concomitant serious cardiopulmonary (New York Heart Association class III or IV; Hugh-Jones dyspnea criteria grade III, IV, or V), hepatorenal, or endocrine disorders; or refusal to participate. It should be noted that in LC procedures with severe acute inflammation, the security and stability of using the Harmonic scalpel is superior to using an electric coagulation hook.[9] For patients who had severe inflammatory or obvious adhesion at the gallbladder triangle that was obvious in preoperative imaging, we usually recommended Harmonic scalpel or open surgery, and they were not included in this clinical trial.

Operative Procedures

All the patients received premedication general anesthesia with endotracheal intubation and intravenous antimicrobial prophylaxis with ceftriaxone sodium as a routine surgical prophylaxis. Laparoscopic cholecystectomy was performed with the standard 3-port technique, as reported earlier[13]; a fourth port was made below the right-side subcostal margin, if necessary. In brief, pneumoperitoneum was established with carbon dioxide insufflation and maintained at 12 mm Hg. Calot's triangle (hepatobiliary triangle or cystohepatic triangle) was dissected with the Harmonic scalpel in the experimental group or by laparoscopic monopolar electrocautery (Force EZ-8C; Valleylab, Boulder, Colorado, USA) in the control group. Closure and sealing of the cystic duct and cholecystic artery were performed with Hem-o-lok clips in both groups. The gallbladder was mobilized from the gallbladder bed, and any obvious oozing blood or bile leak was controlled. A peritoneal drain was inserted into the Morrison's pouch (hepatorenal recess of subhepatic space). The adjustments of the working gear of the Harmonic scalpel were at the sole discretion of the surgeons, and the parameters of monopolar electrocautery were set at 30–45 W for exposing and separating the cystic duct and artery, and 40–50 W for separating the gallbladder from the gallbladder bed.

Postoperative Care and Follow-up

All patients were instructed to resume ambulatory activities and oral intake of a semiliquid diet on postoperative day 1. All patients underwent follow-up abdominal ultrasonography on the day of discharge from the hospital.

Later, all the patients were followed up at the outpatient clinic at 1 week, 1 month, and 6 months after LC, with a physical examination and abdominal ultrasonography.

Main Outcome Measures

The complete data were collected and evaluated by an independent research nurse. The preoperative variables included age, sex, BMI, ASA classification, indication for LC, and concomitant medical and surgical conditions from medical chart review. The operative variables included operative time, estimated blood loss and intraoperative incidents. Intraoperative bleeding was estimated by measuring blood aspirated from the operative field and weighing gauze used for pressure hemostasis. The postoperative variables included postoperative recovery times, postoperative pain, use of postoperative analgesics, postoperative complications, and length of postoperative hospital stay (PHS). The postoperative pain was evaluated at 24, 48, and 72 h after the operation, with the help of a linear visual analog scale (VAS) from 0 (no pain) to 10 points (the most severe pain), with a higher score indicating more serious pain.[14] Postoperative analgesia included 1 dose of intramuscular nonsteroidal anti-inflammatory drug (NSAID) for all patients and an additional dose of NSAID for patients with a VAS score ≥3 points; intramuscular tramadol hydrochloride was given otherwise. The use and dose of analgesics were logged into a medical chart. Postoperative nausea and vomiting were also evaluated after 24 and 48 h of an operation by using a linear VAS from 0 (no nausea/vomiting) to10 points (the most severe nausea/vomiting).[15] Intramuscular metoclopramide was given to prevent any nausea/vomiting if needed. The use and dose of analgesics and antiemetics were recorded in medical charts.

Sample Size Calculation and Statistical Analysis

The sample size was determined for the primary outcome measure using the SPSS program (NCSS Statistical Software, Kaysville, Utah, USA). The statistical analysis was performed using SPSS ver. 12.0 (SPSS Inc., Chicago, Illinois, USA). All the statistical analyses were performed per protocol. The complete continuous data were expressed as means ± SD, and the means were compared by using the 2-independent-sample Student *t*-test. The complete categorical data are expressed as n (%) and compared using Fisher's exact probability test. A 2-tailed $P < .05$ was considered statistically significant.

RESULTS

Out of 287 patients screened for eligibility, 234 patients were randomized to undergo LC with the Harmonic scalpel (n = 138) or monopolar electrocautery (n = 96); 36 patients were excluded from analysis because of withdrawal of informed consent or loss to follow-up (n = 34) or postoperative diagnosis of gallbladder carcinoma (n = 2). Overall, 198 patients were included for the analysis, of whom 117 patients were allocated to the experimental group, and 81 were allocated to the control group (**Figure 1**). Both the groups were comparable with respect to the baseline patient characteristics, including age, sex, BMI, ASA classification, gallbladder disease, and concomitant medical conditions (all $P > .05$; **Table 1**).

Both operative and postoperative data are shown in **Table 2**. Both the groups had similar operative time and blood loss (both $P > .05$). The conversion to open cholecystectomy was required in 1 patient of the experimental group caused by common bile duct injury, whereas none of the patients from the control group underwent conversion ($P > .05$). The major postoperative complications included surgical site infection (1 patient in the control group), postoperative pneumonia (1 patient in the experimental group), and bile leak (1 patient in the experimental group). Both the groups had a similar time length of PHS ($P > .05$), and postoperative pain profile, requirement for analgesics, and postoperative nausea and vomiting profile (all $P > .05$; **Table 3**).

DISCUSSION

According to several studies, the Harmonic scalpel is an effective and safe alternative to monopolar electrocautery for hemobiliary stasis in LC.[9–12] The major advantage of using the Harmonic scalpel in LC over that of conventional monopolar electrocautery is the reduction in operative time. The Harmonic scalpel allows dissection and closure of the cystic artery and ducts <4–5 mm in diameter without requiring clipping (reported by Husceret al[16] in 1999 and certified by the US Federal Food and Drug Administration in 2006), accounting for the reduction in operative time.[17] According to a retrospective case series by Gelmini et al,[18] the use of the Harmonic scalpel in LC is associated with a significantly shorter median operative time, as compared to that of conventional monopolar coagulation: 60 min (range, 20–205 min) vs 85 min (45–150 min); $P < .001$. Zanghi et al[19] also reported in a retrospective study of 164 patients that the use of the Harmonic scalpel is associated with a significantly shorter mean operative time (35 ± 10 vs 56 ± 12 min, $P < .001$);

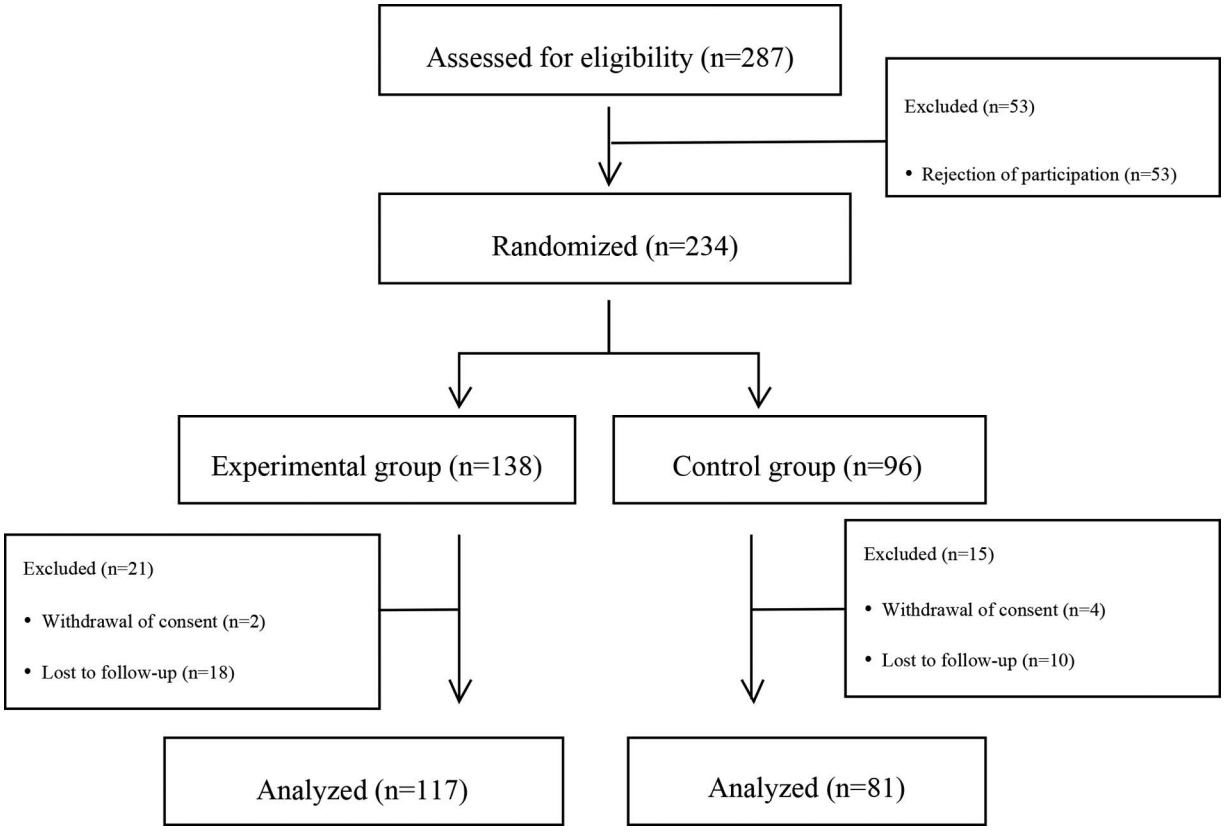

Figure 1. Patient allocation flow chart.

Table 1.
Baseline Characteristics of Per-Protocol Set

	Experimental Group (n = 117)	**Control Group (n = 81)**	***P*-value**
Age, years, mean ± SD	42.2 ± 10.4	43.4 ± 11.1	0.913
Sex, male/female	51/66	40/41	0.421
BMI, kg/m^2, mean ± SD	24.6 ± 3.1	25.0 ± 3.6	0.275
Gallbladder disease, n (%)	103 (88.0)	73 (90.1)	0.348
Polypoid lesion	11 (9.4)	8 (9.9)	
Others	3 (2.6)	0 (0.0)	
Concomitant medical conditions, n (%)			
Cardiac insufficiency	1 (0.8)	0 (0.0)	1.000
Hypertension	5 (4.3)	2 (2.5)	0.776
Liver cirrhosis	1 (0.8)	2 (2.5)	0.747
Diabetes mellitus	2 (1.7)	0 (0.0)	0.514
Depression	0 (0.0)	1 (1.2)	0.409

n = 198.

Table 2.
Operative and Postoperative Data

	Experimental Group (n = 117)	Control Group (n = 81)	*P*-value
Operative time, min, mean ± SD	54.9 ± 13.1	51.7 ± 9.6	0.079
Blood loss, mL, mean ± SD	14.2 ± 10.6	13.7 ± 9.1	0.367
Conversion to laparotomy, n (%)	1 (0.8)	0 (0.0)	0.404
Postoperative complications, n (%)			
Surgical site infection	0 (0.0)	1 (1.2)	0.228
Postoperative pneumonia	1 (0.8)	0 (0.0)	0.404
Bile leak	1 (0.8)	0 (0.0)	0.404
CBD injury	1	0	0.404
PHS, days, mean ± SD	3.0 ± 0.4	2.9 ± 0.4	0.315

n = 198.

Table 3.
Postoperative Pain and Nausea/Vomiting

	Experimental Group (n = 117)	Control Group (n = 81)	*P*-value
Postoperative pain, point, mean ± SD	54.9 ± 13.1	51.7 ± 9.6	0.079
Day 0.5	2.4 ± 0.8	2.3 ± 0.8	0.695
Day 1	1.7 ± 0.7	1.6 ± 0.8	0.020
Day 2	1.7 ± 0.6	1.5 ± 0.7	0.015
Day 7	0.1 ± 0.3	0.1 ± 0.4	0.066
Dose of additional analgesic, mg, mean ± SD			
Day 1			
NSAIDs	0.3 ± 0.7	0.3 ± 0.6	0.484
Tramadol	0.2 ± 0.4	0.2 ± 0.4	0.317
Day 2			
NSAIDs	0.03 ± 0.18	0.04 ± 0.19	0.832
Postoperative nausea/vomiting, point, mean ± SD			
Day 1	2.7 ± 1.2	2.7 ± 1.2	0.915
Day 2	2.0 ± 1.2	1.9 ± 1.2	0.473
Day 3	1.4 ± 0.8	1.2 ± 0.7	0.527

n = 198.

and Kandil et al[9] reported in a prospective, randomized study that the use of the Harmonic scalpel alone for dissection and sealing in LC resulted in almost half the mean operative time (33.2 ± 9.6 vs. 51.7 ± 13.8 min, $P = .001$). This benefit was thought to result from there being no requirement for laparoscopic instrument exchange and the absence of surgical smoke in the operative field from the use of the Harmonic scalpel.[18,20] However, Bulus et al[21] reported in 60 patients who underwent LC with the Harmonic scalpel, bipolar vessel sealing, and monopolar electrocautery that the use of any of these 3 surgical dissection or coagulation instruments was not associated with a clinically significant increase or reduction in mean operative time (33 ± 10 vs 32 ± 11 vs 37 ± 10 min,

respectively). Catena et al[12] further showed in a prospective, randomized, single-center study regarding LC for acute cholecystitis that the Harmonic scalpel or electrocautery techniques had similar mean operative times (101.3 vs 106.4 min; $P > .05$). This inconsistency in the operative time may be the result of variations in the study protocol, patient selection, operative technique, surgeon's experience, and case volume. Our results showed that the use of conventional monopolar electrocautery was equal to that of the Harmonic scalpel with respect to the operative time of simple LC in the hands of experienced laparoscopic surgeons. It should be noted that, in the experimental and control groups, the cystic duct and artery were closed with Hem-o-lok clips. This result may contrast with that obtained when surgeons use the Harmonic scalpel to close the cystic duct and artery directly in LC.

LC using conventional monopolar electrocautery is well documented to be safe and associated with occasional iatrogenic injury, such as postoperative bleeding, bile duct damage and bowel perforation, mainly because of the effect of collateral energy from electrocauterization, in contrast to minimal energy transfer from ultrasonic vibration. According to some previous studies, the use of the Harmonic scalpel may be associated with a reduced risk of conversion to open procedure and overall surgical morbidity, compared with conventional electrocautery. However, the lower risk was not statistically or clinically significant in these studies.[9–12] Our study results reaffirmed that the use of conventional monopolar electrocautery was not associated with a significantly higher risk of conversion and surgical morbidity when compared with that occurring with the Harmonic scalpel. The major factors contributing to LC conversion to laparotomy and other surgical morbidity included laparoscopic dissection difficulty or gallbladder perforation caused by adhesion, uncontrollable bleeding, bile leak, missed coexisting bile duct stones, or gallbladder cancer on preoperative assessment and concomitant medical or surgical conditions.[22] Thus, the use of the Harmonic scalpel or monopolar electrocautery does not have a significant impact on conversion or surgical morbidity, provided the aforementioned confounding or complicating factors are well balanced or excluded, as in our uncomplicated patients scheduled for LC. However, the use of the Harmonic scalpel resulted in the highest cystic-duct–bursting pressure.[23] This complication occurred in a case of choledochus injury with conversion to laparotomy in our experimental group. It was mainly caused by a mistake in intraoperative identification of a deformity of the biliary tract, but the use of the Harmonic scalpel with its inability to performing fine dissection with the bulky tip and difficulty in manipulation of the tissue plane with a straight tip also carries potential risks.

Reduced postoperative pain and expedited postoperative recovery are major well-documented advantages of LC over an open procedure, apart from its favorable aesthetic outcome, mainly because of the minimal invasiveness of the port site incision in LC. The post-LC pain may be caused by residual pneumoperitoneum, diaphragm stretching and long-time laparoscopic manipulation. In previous studies reporting the use of the Harmonic scalpel with less postoperative pain, the major cause may be a significantly shorter operative time for LC with a Harmonic scalpel than with monopolar electrocautery.[9] However, our study results showed that the 2 techniques were associated with similar post-LC pain, requirement for analgesics, and postoperative nausea and vomiting, probably because both the techniques were associated with a similar operative time in our uncomplicated patients. Consequently, the use of the Harmonic scalpel did not offer an additional benefit in postoperative recovery.

There were certain limitations in this study. First, patient allocation was not blinded to the investigators, whereas the randomization scheme was carried out by a central procedure and the patient data were collected and evaluated by independent research staff. Second, the noninferiority of using conventional monopolar electrocautery to using Harmonic scalpel might be subject to an investigator's bias, because the authors are more experienced in the use of monopolar electrocautery: this is known as the learning curve effect; however, this effect applies to all the general surgeons performing LC. Third, an additional benefit of using the Harmonic scalpel for LC may be underestimated, especially in patients with comorbidities, such as those with cirrhosis,[24] as these patients were excluded from this study, whereas nearly all the patients scheduled for LC had no comorbidities.

In conclusion, the use of the Harmonic scalpel for LC in the treatment of uncomplicated cases was associated with similar operative time, conversion risk, blood loss, and postoperative recovery when compared with LC using conventional monopolar electrocautery in the hands of experienced surgeons. The major limitation in using the Harmonic scalpel is its relatively high cost, especially in underprivileged practices. The use of the harmonic scalpel may be preferred in selected patients with a high risk of surgical morbidity. The increased cost and negligible benefits shown in this study make it inadvisable to use the Harmonic scalpel in uncomplicated LC when compared with monopolar electrocautery.

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