Dissection by Ultrasonic Energy Versus Monopolar Electrosurgical Energy in Laparoscopic Cholecystectomy

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ABSTRACT

Introduction: Laparoscopic cholecystectomy is the gold standard for management of symptomatic gallstones. Electrocautery remains the main energy form used during laparoscopic dissection. However, due to its risks, search is continuous for safer and more efficient forms of energy. This review assesses the effects of dissection using ultrasonic energy compared with monopolar electrocautery during laparoscopic cholecystectomy.

Methods: A literature search of the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library, MEDLINE, and EMBASE was performed. Studies included were trials that prospectively randomized adult patients with symptomatic gallstone disease to either ultrasonic or monopolar electrocautery dissection during laparoscopic cholecystectomy. Data were collected regarding the characteristics and methodological quality of each trial. Outcome measures included operating time, gallbladder perforation rate, bleeding, bile leak, conversion rate, length of hospital stay and sick leave, postoperative pain and nausea scores, and influence on systemic immune and inflammatory responses. For metaanalysis, the statistical package RevMan version 4.2 was used. For continuous data, Weighted Mean Difference (WMD) was calculated with 95% confidence interval (CI) using the fixed effects model. For Categorical data, the Odds Ratio (OR) was calculated with 95% confidence interval using fixed effects model.

Results: Seven trials were included in this review, with a total number of 695 patients randomized to 2 dissection methods: 340 in the electrocautery group and 355 in the ultrasonic group. No mortality was recorded in any of the trials. With ultrasonic dissection, operating time is significantly shorter in elective surgery (WMD -8.19, 95% CI -10.36 to -6.02, P<0.0001), acute cholecystitis (WMD -17, 95% CI -28.68 to -5.32, P=0.004), complicated cases (WMD -15, 95% CI -28.15 to -1.85, P=0.03), or if surgery was performed by trainee surgeons who had performed <10 procedures (P=0.043). Gallbladder perforation risk with bile leak or stone loss is lower (OR 0.27, 95% CI 0.17 to 0.42, P<0.0001 and OR 0.13, 95% CI 0.04 to 0.47, P=0.002 respectively), particularly in the subgroup of complicated cases (OR 0.24 95% CI 0.09 to 0.61, P=0.003). Mean durations of hospital stay and sick leave were shorter with ultrasonic dissection (WMD -3.8, 95% CI -6.21 to -1.39, P=0.002 respectively), with a smaller mean number of patients who stayed overnight in the hospital (OR 0.18, 95% CI 0.05 to 0.89, P=0.04). Postoperative abdominal pain scores at 1, 4, and 24 hours were significantly lower with ultrasonic dissection as were postoperative nausea scores at 2, 4, and 24 hours.

Conclusion: Based on a few trials with relatively small patient samples, this review does not attempt to advocate the use of a single-dissection technology but rather to elucidate results that could be used in future trials and analyses. It demonstrates, with statistical significance, a shorter operating time, hospital stay and sick leave, lower gallbladder perforation risk especially in complicated cases, and lower pain and nausea scores at different postoperative time points. However, many of these potential benefits are subjective, and prone to selection, and expectation bias because most included trials are unblinded. Also the clinical significance of these statistical results has yet to be proved. The main disadvantages are the difficulty in Harmonic scalpel handling, and cost. Appropriate training programs may be implemented to overcome the first disadvantage. Cost remains the main universal issue with current ultrasonic devices, which outweighs the potential clinical benefits (if any), indicating the need for further cost-benefit analysis.

Key Words: Ultrasonic dissection, Electrocautery, Electrosurgical energy.

INTRODUCTION

Since 1987, laparoscopic cholecystectomy has evolved to become the gold standard for management of symptom-
atic gallstones. Electrocautery remains the main energy form used during laparoscopic dissection. However, because of its documented risks, especially those related to visceral injury, search for alternative forms of energy that can be used in laparoscopic dissection and even coagulating and sealing vessels and ducts began very early during the evolution of laparoscopic cholecystectomy itself, specifically in 1992 by researchers such as Wetter. Among these alternative energy sources are ultrasonic energy and laser energy. For various reasons, neither have gained widespread acceptance among surgeons for routine or emergency laparoscopic cholecystectomy. This review investigates the possible beneficial aspects and disadvantages of ultrasonic dissection compared with monopolar electrocautery.

**METHODS**

A literature search was performed for studies in which patients were randomized to 1 of the 2 dissection techniques. Databases used included the Cochrane Central Register of Controlled Trials (CENTRAL - the Cochrane Library issue 3, 2008), MEDLINE [using Medical Subject Heading (MeSH) terms], and EMBASE. There were no limitations with regards to sample size, blinding, language, or publication status.

All reports in which there is a direct comparison between at least 2 dissecting techniques have been reviewed and only prospective randomized studies that compared ultrasonic dissection with monopolar electrocautery dissection in laparoscopic cholecystectomy were included in meta-analysis. Seven trials fulfilled the study criteria, including a total of 695 patients; 355 in the ultrasonic group and 340 in the electrocautery group.

As with other new technologies, it was not possible to prevent or avoid possible editorial bias. Therefore, we cannot be certain that the included “published” trials are the only randomized trials reporting ultrasonic dissection versus monopolar electrocautery in laparoscopic cholecystectomy.

It follows that the results and conclusions of this review are limited only to these 7 included trials and should be viewed in that way.

With regards to electrocautery, all included trials studied the monopolar type. However, some studied the electrocautery “hook,” and others reported dissecting scissors or forceps that are connected to an electrocautery source.

Ultrasonic dissection was reported using different devices and terminology [Harmonic scalpel, ultrasonic shears, ultrasonically activated coagulating shears (UACS), Ultrasonic Harmonic Shears (UHS), and Cavitron Ultrasonic Surgical Aspirator (CUSA)]. Some of these devices have major structural differences, but others only have minimal design differences. Despite these differences, however, the basic mechanism of ultrasonic coagulation is the same, and this makes the comparison possible with electrocautery that works by a different mechanism, provided that the operative conditions are standardized.

Patients in this review are adults with symptomatic gallstones who underwent laparoscopic cholecystectomy. Most studies excluded patients with acute cholecystitis. In one study, however, participants who were found to have features of acute cholecystitis during surgery were excluded but were reported in the study results. These cases among the elective cases will also be analyzed in this review.

In some trials, clear exclusion criteria were stated. Examples of these are patients who had previous abdominal surgery, pregnant patients, patients with a suspicion of gallbladder cancer based on abdominal ultrasound scan and a subsequent CT scan, and patients with common bile duct stones or immune suppression.

Several outcomes are discussed in the reviewed trials. Operating time is a main outcome studied in most of the included trials. In one additional study, operating time was considered as a secondary outcome with gallbladder perforation being the primary focus of that study. In all 5 studies, operating time is expressed in minutes.

Gallbladder perforation during dissection from the liver bed is the main endpoint in 2 reports (where it was expressed by the number of patients affected). This was considered of 2 categories: either gallbladder perforation with biliary leak only or perforations associated with stone loss into the peritoneal cavity. Bleeding was one of the main outcomes in 2 reports. Consideration of this outcome, however, was presented in a different way in each study. In one report, blood loss was considered as an “amount” and was measured in milliliters (mL). In the second study, blood loss was described as significant only if it was more than 10mL in amount.

Postoperative bile leakage was discussed in 2 trials.
was defined as bile continuing to be observed in the subhepatic drain during the postoperative stage for a certain period of time.3

Conversion to open surgery or to another laparoscopic procedure was discussed in several trials; Cengiz7 reported conversions in 7 patients who were excluded from further analysis. There were several stated reasons for this including “severe cholecystitis, choledocholithiasis, and suspected gallbladder cancer”.7 In another trial,8 only 1 patient underwent conversion to an open procedure, and 5 other patients needed to have laparoscopic exploration of the common bile duct. Two patients underwent conversion to open procedures in a third trial due to “intraperitoneal adhesions and extensive periportal scarring.”2

Postoperative pain and nausea scores were estimated in one study by using the 10-point visual analogue scale at 1, 2, 4, and 24 hours after surgery.7 Mean pain scores were also used in a second study without the type of scales used being mentioned, but with further analyzing pain as either abdominal or shoulder pain.3 For assessment of nausea, one trial used the number of patients suffering from postoperative nausea as an outcome indicator instead of a scale score, and added “vomiting” as another associated outcome indicator that was measured in the same way.3

Length of hospital stay (LHS) was described as either the mean number of days during which patients stayed in hospital2,3 or in terms of the mean number of patients who needed overnight hospital stay for particular reasons.7 In either case, LHS was an important outcome parameter, albeit not the primary one. Some studies did not consider this outcome in their results.4–6,8

Sick leave was the standard outcome in only 2 trials.2,7 In one study, “patients decided their own length of sick leave but asked to return to work as soon as possible.”7 In case of unemployed patients, it was left to their own discretion to estimate the length of the sick leave in the context of their previous occupation.7

Among the nonclinical outcomes studied by some of the selected trials was the influence on systemic immune response and expression of transforming growth factor beta-1. In the trial by Sietses et al.,4 effects of dissection methods on systemic immune response were studied. A further trial by Brokelman et al.5 investigated perioperative peritoneal expression of transforming growth factor beta-1 (TGF-β1) in laparoscopic cholecystectomy when the 2 dissection methods were used.5 TGF-β1 is an important stimulant of peritoneal adhesiogenesis through stimulating production of plasminogen activator inhibitor-1 (PAI-1), which is the main inhibitor of fibrinolysis.9

**Methodological Quality**

All 7 studies are prospective randomized trials that compared 2 broad types of gallbladder dissection: ultrasonic (as a method under investigation) and monopolar electrocautery (as the standard method currently used in practice). Wetter,2 however, also included a third dissection method in his comparisons, which is laser dissection. This group of patients and all their related data are not included here. This review did not consider the detailed differences in the ultrasonic technology used in different trials and considered the results of all forms of ultrasonic dissection collectively as a single group in subsequent comparisons. The reason is that the basic mechanism in coagulating and fragmenting tissues with ultrasonic energy is the same despite differences in devices. The structural design of the Cengiz trial was of particular concern.7 Comparison in that report was made between traditional gallbladder dissection (with dissection starting at Calot’s triangle) and ultrasonic fundus-first dissection. Patients were assigned to 2 groups, while it would be ideal to randomize them into 4 groups according to the dissection method and the dissection technique (classical or fundus-first). This concern was also mentioned by Decadt.10

Three main aspects of methodological quality were studied: sample size, randomization, and blinding.

**Sample size** calculation was outlined in 2 trials; Janssen et al.8 and Cengiz et al.7 In the former study, calculations were based on test power (1 – β) of 80%, significance level (α) at 5% (P<0.05), and a difference of 25% in operating time and length of sick leave (the 2 main postulated outcomes in that study). In the later report, sample size calculation was based on the same power and significance levels and on the assumption of a 35% reduction in the rate of gallbladder perforation by ultrasonic dissection (note that gallbladder perforation is the main outcome in that study). However, both studies did not explain on which basis such differences were made in the operating time, duration of sick leave, or in the gallbladder perforation rate, because there had been no pilot studies. Other reports failed to discuss their sample size calculations (if any). In a personal correspondence with Bessa, the author stated that there were no previous pilot studies in the subject of his trial6 to accurately calculate a sample size.

Following the CONSORT recommendations,11 3 issues with randomization were looked at in this review; allo-
cation sequence generation (ASG), allocation concealment (AC), and implementation of randomization (IR).

ASG is unclear in all 7 trials. Despite declaring random allocation of patients, none of the authors explained how the allocation sequence was generated. This might not be a design flaw in any of the trials, but rather an inadequate presentation of the methods. In addition, despite the aspect of studying the feasibility of ultrasonic dissection to surgical trainees in Janssen’s trial, stratification for experience in laparoscopic cholecystectomy was not performed without explaining the reasons in the report. We should not, however, consider the randomization methods in any of the 7 trials inadequate, as neither of the authors admitted using quasi-randomization methods (names, dates, alternating weeks, and other such things), and lack of stratification does not subvert randomization.

AC method was mentioned in 5 studies. Patients were randomized using sealed envelopes that were opened either after the initiation of anesthesia, just before surgery, or once the decision was made to proceed with surgery. Sealed envelopes are considered an adequate method of concealment.

IR is considered as “adequate” if ASG patient enrollment and patient assignment (to the groups) were all carried out by a person(s) or a body totally independent of the research group. Unfortunately, all included trials failed to explain the method of implementation of their patient allocations, therefore, rendering their IR “unclear.”

Blinding of the clinicians is essential to avoid performance and expectation bias. However, blinding of surgeons is not possible, but blinding is possible in patients, nurses, and caregivers. Despite this, only Cengiz and coauthors attempted blinding of patients and nurses. In principle, blinding of patients and caregivers (as opposed to surgeons) should be adequate if this is declared in the trial and the method of blinding is described. If blinding was declared but not explained, we would consider this as unclear. Blinding should be considered as absent or “not performed” if it was not clearly declared by the authors in their methods.

Statistical Method

For pooling of data and metaanalysis, the statistical package of RevMan version 4.2 was used. For continuous data, Weighted Mean Difference (WMD) was calculated with 95% confidence interval using the fixed effects model. For Categorical data, Odds Ratio (OR) was calculated with 95% confidence interval using the fixed effects model. Funnel plots were produced to investigate the possibility of publication bias or other factors that might cause bias of analyses results.

RESULTS

Despite heterogeneity in the methods of the included trials, it was possible to combine sets of data for 6 outcomes: operating time for elective laparoscopic cholecystectomy, gallbladder perforation with bile leak only, mean length of hospital stay, number of patients who needed overnight hospital stay, mean duration of sick leave, and abdominal pain scores at 24 hours postoperatively.

As shown in Figure 1, the point estimate of the 5 included trials shows no statistically significant difference in mean patient age in the comparison groups ($P=0.57$). Heterogeneity between included trials was statistically significant.

Operating time is significantly shorter in elective laparoscopic cholecystectomy when ultrasonic dissection is used. Figure 2 shows a point estimate that favors the ultrasonic dissection with effect estimate (WMD) of -8.19.
(95% CI -10.36 to -6.02). Heterogeneity between studies was statistically insignificant \( \chi^2 = 0.65, \text{df} = 2 (P = 0.72) \). Furthermore, in the Janssen trial,\(^8\) the mean operating time was significantly shorter in ultrasonic versus electrocautery groups:

- When surgery was performed by the least experienced surgeons (who performed <10 laparoscopic cholecystectomies): 66.7 (range, 45 to 95) minutes versus 85.4 (range, 60 to 180) minutes (\( P = 0.043 \)).\(^8\)

- When operating on patients with complicated gallbladders (e.g., distended gallbladders, adhesions): 60 (range, 28 to 120) minutes versus 80 (range, 32 to 180) minutes (\( P = 0.049 \)).\(^8\)

Most trials excluded patients with acute cholecystitis.\(^2-6,8\) Only Cengiz et al\(^7\) discussed differences in operating time in acute cholecystitis separately. The Mann-Whitney U test was used to calculate \( P \) value (0.004). This trial concluded that, in acute cholecystitis, the operating time is significantly shorter using the laparoscopic fundus-first technique with ultrasonic dissection (WMD -17, 95% CI -28.68 to -5.32, \( P = 0.004 \)).

Complicated cases were included in the Janssen trial.\(^8\) These are patients with hydrops of the gallbladder, gallbladder shrinkage, stones trapped in the cystic duct, and adhesions around the gallbladder.\(^8\) Interestingly, ultrasonic dissection was associated with a shorter mean operating time in this subgroup compared with electrocautery, with a statistically significant difference (WMD -15.00, 95% CI -28.15 to -1.85, \( P = 0.03 \)).

Detailed data on operating time with and without gallbladder perforation were only described by Bessa.\(^6\) The majority of patients did not have gallbladder perforation during dissection, and the operating time was found to be statistically shorter in the ultrasonic group knowing that clipless technique was used in this group (WMD -4, 95% CI -6.48 to -1.52, \( P = 0.002 \)). Six of 60 patients had gallbladder perforations in the ultrasonic group compared with 20 of 60 patients in the electrocautery group. To illustrate the effect of gallbladder perforation on the operating time in both comparison groups, the mean operating time (±SD) was 59.2(14) minutes and 61.9(12.2) minutes, respectively, and the difference was not statistically significant (\( P = 0.26 \)).\(^6\)

Gallbladder perforation with bile leak, stone loss, or both, was discussed in 3 trials.\(^3,6,8\) Thirty out of 256 patients had gallbladder perforations with bile loss in the ultrasonic group compared with 86 out of 263 patients in the electrocautery group. This is statistically significant (OR 0.27, 95% CI 0.17 to 0.42, \( P < 0.00001 \)) (Figure 3). There is no statistically significant heterogeneity between the trials \( \chi^2 = 3.89, \text{df} = 2 (P = 0.14) \). In the Janssen trial,\(^8\) although there was a significant difference in the gallbladder perforation rate with subsequent bile leak between junior trainees (who performed ≤20 procedures) and more senior surgeons, in favor of the seniors when monopolar electrocautery was used for dissection (\( P = 0.026 \)), there was no statistical difference in that outcome between juniors and seniors when ultrasonic dissection was used.

The number of gallbladder perforations with stone loss was only described by Janssen et al.\(^8\) Three out of 96 patients had gallbladder perforation along with stone loss in the ultrasonic dissection group compared with 20 out of 103 patients in the electrocautery group. This is a statistically significant difference (OR 0.13, 95% CI 0.04 to 0.47, \( P = 0.002 \)).

The number of gallbladder perforations in complicated cases was also described by Janssen et al.\(^8\) Examples of complicating factors include adhesions, cystic duct stone(s), and distended gallbladders. Forty-five patients in

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**Figure 2.** Operating time in minutes (\( P < 0.00001 \)).
the Ultracision group (n = 96) had complicating factors compared with 51 in the electrosurgery group (n=103). Ultrasonic dissection resulted in a significantly lower number of perforations compared with electrosurgery (OR 0.24, 95% CI 0.09 to 0.61, P = 0.003).

Postoperative bile leakage was only discussed in 2 trials.3,6 No patients had subhepatic drains or postoperative bile leakage in the ultrasonic group (n=160), while in the electrosurgery group (n=160), 3 patients had bile observed in their subhepatic drains reported by Tsimoyiannis et al.3 In 2 patients, bile leakage was observed during the first 24 postoperative hours, while in the third patient, bile leakage continued for 6 days. In all, endoscopic retrograde cholangiopancreatography (ERCP) confirmed bile leakage from the gallbladder's liver bed.3 There is no statistical difference between the 2 groups with regards to this outcome (P=0.19) despite the claim in other reports that Harmonic scalpel dissection of the liver bed can more effectively close the ducts of Luschka11 (Figure 4).

A total of 13 patients were excluded due to conversion; some from the analysis only2,7 or from the whole trial and randomly replaced by new patients.5 Conversion to open surgery was not considered in another study that looked at clinical outcomes,8 or looked for them but they simply did not occur.5 Trials, such as those of Sietses et al4 and Brokelman et al5 have legitimately ignored this outcome as both have looked at surrogate rather than clinical outcomes. Therefore, only 2 reports have determined the number of conversions in each arm of the study6,7; hence, we were able to compare the conversion rate, which is not statistically different in a total of 200 patients (Figure 5).

In 2 trials, subhepatic closed drains were left for the first 24 postoperative hours either in all patients,6 or in patients who were likely to ooze blood or to have bile leakage. A total of 26 patients in the ultrasonic dissection group (n=100) had subhepatic drains, compared with 37 patients in the electrosurgery dissection group (n=100).8 The difference in the need for...
subhepatic drains in the immediate postoperative period was statistically insignificant.

The mean length of hospital stay (LHS), in days, is discussed in 5 trials.\(^2\)-\(^4\),\(^6\),\(^7\) It was determined by the patients needs and speed of postoperative recovery except in 2 trials, where patients were kept in the hospital for 1 or 2 postoperative days as a part of their protocols.\(^4\),\(^6\) A total of 246 patients had ultrasonic dissection compared with 223 patients who had dissection by monopolar electrocautery. Based on Tsimoyannis et al results,\(^3\) there is a statistically significant shorter LHS with ultrasonic dissection (WMD \(-0.3, 95\%\ CI -0.51\) to \(-0.09, P<0.005\)) (Figure 6). Nevertheless, it is important to emphasise that, in unblinded studies, such as that of the Tsimoyiannis et al trial,\(^3\) LHS is prone to unconscious bias, manipulation, or both.

The mean duration of sick leave was discussed in 2 trials.\(^2\),\(^7\) A total of 77 patients who had ultrasonic dissection were compared with 54 patients who had electrocautery. There is a statistically significant shorter duration of sick leave with ultrasonic dissection compared electrocautery, (WMD \(-3.8, 95\%\ CI -6.21\) to \(-1.39, P=0.002\)) (Figure 7).

Postoperative pain scores studied in the Cengiz et al trial\(^7\) at the first and fourth hours of recovery are statistically lower with ultrasonic dissection (WMD \(-1.10, 95\%\ CI -2.16\) to \(-0.04, P=0.04\) and WMD \(-0.80, 95\%\ CI -1.34\) to \(-0.26, P=0.004\)).\(^7\) Pain scores at 24 hours of recovery from Cengiz and Tsimoyiannis trials were combined with a lower estimate in the ultrasonic dissection group (WMD \(-0.94, 95\%\ CI -1.06\) to \(-0.82, P<0.00001\)).\(^3\),\(^7\) Heterogeneity between trials is statistically significant \([\gamma^2 =41.18, df =1, P<0.00001]\) (Figure 8).

Postoperative nausea scores at 2, 4, and 24 hours were statistically lower with ultrasonic dissection (WMD \(-0.90, 95\%\ CI -1.62\) to \(-0.18, P=0.01\), WMD \(-0.80, 95\%\ CI -1.31\) to \(-0.29, P=0.002\), and WMD \(-1.20, 95\%\ CI -2.02\) to \(-0.38, P=0.004\), respectively), while there was no statistical difference in the number of patients who experienced a clinically significant postoperative nausea,\(^3\) nor was there a statistical difference in the number of patients who suffered from vomiting in the early postoperative period (P=0.65).\(^3\)

Postoperative suppression of immune function was discussed in detail only in the Sietses et al trial.\(^3\) With a small sample size (n=18), he compared the preoperative and

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**Figure 5.** Rate of conversion to open surgery (p= 0.55).

**Figure 6.** Mean LHS in days (p= 0.005).
postoperative levels of HLA-DR expression within each group and between the 2 dissection groups, with no statistical difference.

In the same trial conducted by Sietses and co-researcher, measurement of the postoperative inflammatory response was expressed by the preoperative and postoperative levels of C-reactive Protein (CRP) and the white cell count (WCC). CRP levels were expectedly significantly higher in both groups postoperatively, but postoperative mean CRP levels were not significantly different between the 2 dissection groups (P = 0.95).

Preoperative mean WCC were recorded by 2 trials in both the ultrasonic and dissection groups. There is no statistically significant difference in WCC between ultrasonic and electrocautery dissection groups during the first postoperative day (P = 0.58).

Perioperative levels of peritoneal growth transforming factor beta-1 (GTF-β1) expression was only discussed by Brokelman in his trial on GTF-β1 peritoneal expression during laparoscopic cholecystectomy. GTF-β1 levels were measured both at the start and at the end of the procedures in 2 randomized groups (n=10 each) with equal intraabdominal pressures and lighting. The finding that ultrasonic scalpel dissection is associated with lower peritoneal total and active GTF-β1 levels compared with electrocautery (P<0.005 and P<0.01, respectively) at the end of the surgery, suggests a reduced risk of peritoneal adhesion formation with the former dissection device.

Postoperative complications were described in 2 studies. In total, there were 10 patients who experienced postoperative complications out of 320 patients (3.1%). In the ultrasonic group, only 3 of 160 patients had complications (1.9%) compared with 7 in the electrocautery group (4.4%). The difference in the overall postoperative complication rate is not statistically significant (OR 0.45, 95% CI 0.12 to 1.65, P = 0.23). There is no significant heterogeneity between the 2 trials (P = 0.32) (Figure 7).

As described by Tsimoyiannis et al, there were no patients with postoperative bile leakage in the ultrasonic group (n=100), compared with 3 patients in the electrocautery group (n=100). In 2 patients, bile leakage was observed during the first 24 postoperative hours, while in the third patient, bile leakage continued for 6 days. In all, endoscopic retrograde cholangiopancreatography (ERCP) confirmed bile leakage from the gallbladder’s liver bed. The Bessa et al trial, no minor or major bile leaks were reported in the drains postoperatively, but the authors did report port-site and chest infections in 5 and 2 patients, respectively. Port-site infections occurred in 2 patients in

Figure 7. Mean duration of sick leave in days (p = 0.002).

Figure 8. Postoperative pain scores at 24 hours (p < 0.00001).
the ultrasonic group (3.3%) and in 3 others in the electrocautery group (5%). The incidence of chest infection was equal in both groups (1 patient in each arm or 1.6%).

**DISCUSSION**

Ultrasonic dissection technology works by generating a high-frequency ultrasound (eg, 55000 cycles/second) and applying such energy to the tissues producing 3 main “C” effects:

1. Cavitation/tissue fragmentation (and dissection)—caused by cellular destruction secondary to intracellular fluid evaporation, and this occurs due to “low pressure at the blade”. Cavitation is an important effect of ultrasonic energy, because it causes separation of tissue planes facilitating dissection. This is particularly useful when looking for the “correct” plane of dissection between the liver and the gallbladder.

2. Cooptation/coagulation: caused by conversion of ultrasonic energy into a localized heat, this has been reported to reach to 60°C to 100°C. Denaturation of collagen in the walls of hollow structures (such as cystic artery and duct) can result in the occlusion or sealing of the lumen. The mechanism occurs when ultrasonic energy is transferred to tissue. This breaks the tertiary hydrogen bonds between the collagen and the proteins of extracellular matrix. These proteins denature and change from colloidal proteins into an insoluble gel that is able to seal the vessel walls. This gel coagulation is specific to ultrasonic dissection, and the airtight pressure of a sealed cystic duct was calculated to be “higher than 320mm Hg”.

3. Cutting—which is achieved by the “sharp” blade mode of the Harmonic scalpel.

It has been reported that with ultrasonic energy, there is a minimal lateral spread of vibration current in the surrounding tissues minimizing the risk of injury compared with monopolar electrocautery, which is associated with 90% of visceral injuries and 15% of biliary tract injuries during laparoscopic cholecystectomy.

Three animal studies confirmed the increased lateral spread of thermal energy from monopolar electrocautery and subsequent increased tissue injury compared with ultrasonic energy. Safety of electrosurgical devices may also be compromised by the possible failure of insulation of the active electrode, which may lead to electrical “coupling” with other surgical instruments or tissue with subsequent generation of stray electrical current. However, in a more recent controlled animal trial, monopolar electrocautery produced negligible thermal injury in the extrahepatic biliary ducts after laparoscopic cholecystectomy.

Although some authors argue that the safety of the ultrasonic dissector may be enhanced by the reduced need for instrument replacement during surgery, others demonstrated that ultrasonic dissection is not as safe because it has been initially perceived.

Tebala argues that because the Harmonic scalpel can replace 4 instruments [scissors, clipper, dissector (such as Maryland dissector), and electrocautery hook], and because that in the classical technique using electrocautery, frequent change (extraction and reinserterion) of instruments can increase the risk of tissue injury, such as bowel or liver, multiple functions of the Harmonic scalpel may eliminate the need for instrument change, thus reducing the risk of tissue injury. While this could be true, the risk of tissue injury by ultrasonic dissection remains clear and was demonstrated by others. An experimental animal study by Emam and Cuschieri showed that high-power ultrasonic dissections resulted in considerable heat production that caused proximal collateral damage to adjacencies.
cent tissues when continuous activation time exceeded 10 seconds.

Because data are conflicting regarding the potential benefits and risks of ultrasonic dissection in laparoscopic cholecystectomy, this review attempts to further explore such outcomes that could be related to tissue handling and any resulting tissue injury.

However, it should be emphasized that this review is limited by several factors, including the small number of eligible trials and the relatively small number of patient samples, and also by the fact that not all analyzed studies looked at the same endpoint(s).

The duration of operating time is statistically shorter with ultrasonic dissection not only in elective laparoscopic cholecystectomy ($P < 0.0001$), but also when operating on patients with acute cholecystitis ($P = 0.004$), and on complicated cases ($P = 0.03$), or if surgery is performed by trainee surgeons who have performed <10 procedures ($P = 0.043$). This statistical significance does not necessarily mean a clinical advantage, especially when operating time is largely dependent on the training and expertise of individual surgeons. Most surgeons can improve their use of monopolar electrosurgery, which will shorten their operating time, while ultrasonic dissection by the inexperienced hands may well be a long, unsafe dissection procedure.

Gallbladder perforation risk with bile leak, stone loss, or both, is lower with ultrasonic dissection ($P < 0.0001$ and $P = 0.002$, respectively), and in the subgroup of complicated cases, the risk of perforation is significantly lower ($P = 0.003$). The mean length of hospital stay is statistically shorter with ultrasonic dissection compared with electrosurgery ($P = 0.005$), so is the smaller mean number of patients who stayed overnight in the hospital ($P = 0.04$). Moreover, the mean duration of sick leave after laparoscopic cholecystectomy using ultrasonic dissection is significantly shorter compared with surgery using electrosurgery dissection ($P = 0.002$). The length of hospital stay and overnight stay are more likely prone to performance and expectation bias in unblinded studies. Patients, caregivers, and nurses were blinded in the Cengiz trial, the trial that showed a significantly smaller number of patients staying overnight. However, clearly surgeons were not blinded, and whether this influenced the decision to keep or discharge patients is not clear, although the authors claimed that this was entirely the decision of the ward nurse (who was blind to the dissection method used).

Postoperative abdominal pain scores at 1, 4, and 24 hours are significantly lower with ultrasonic dissection but with heterogeneity between studies, while postoperative nausea scores at 2, 4, and 24 hours are significantly lower with ultrasonic dissection compared with electrosentry ($P = 0.01$, $P = 0.002$, and $P = 0.004$, respectively).

The risk of postoperative formation of adhesions may be significantly lower with ultrasonic dissection. The finding by Brokelman et al that ultrasonic scalpel dissection is associated with lower peritoneal total and active GTF-β1 levels compared with electrosurgery ($P < 0.005$ and $P < 0.01$, respectively) at the end of surgery, suggests a reduced risk of formation of peritoneal adhesions with the former dissection device. However, this study is not sufficient to prove this potential benefit, because this would require a head-to-head comparison as well as second-look laparoscopy for verification.

Due to the short postoperative follow-up periods in some of the included trials and its absence in others, the true risk of delayed biliary complications remains unclear, and this may outweigh the potential benefits of ultrasonic dissection. However, there is evidence from the Bessa et al trial showing the absence of this risk. Also, none of the patients in a trial by Huscher et al has suffered from postoperative biliary stricture during a maximum follow-up period of 6 months as determined by ultrasound scanning.

The main disadvantage of ultrasonic dissection is instrument cost, which is particularly true if the surgical unit is equipped with reusable instruments. Nevertheless, some authors believe that compared with combined cost of using multiple disposable instruments (scissors, a clipper, an electrosurgical hook, and a grasper), the Harmonic scalpel may provide a cost-effective option.

In a cost analysis by Westervelt, the cost in an American hospital of a disposable LCS Harmonic scalpel blade tip is $350.00. This is compared with the combined cost of a disposable electrosurgery shears and a clipper, which is $350.00. In Europe, Huscher et al estimated the cost for a disposable LCS Harmonic scalpel to be lower compared with the combined cost for one scissors and one clipper (346.03 Euro vs. 397.67 Euro).

However, the cost issue is relevant only on the assumption that disposable technology is used for monopolar electrosurgery. By knowing that both ultrasonic and monopolar electrosurgery are now reusable instruments, making cost comparisons would be more difficult. It is therefore advocated that further comparative studies should be carried out preferably within a single health system or even within a single health institution.
CONCLUSION

It is important to emphasise that the conclusions of this review are based on a few trials with a relatively small patient sample. It does not attempt to advocate the use of a single dissection technology but rather to elucidate results that could be used in further trials and analyses. This review demonstrates—with statistical significance—a shorter operating time, hospital stay, and sick leave, lower gallbladder perforation risk especially in complicated cases, and less pain and nausea scores at different post-operative time points.

However, many of these potential benefits are variable, subjective, and largely prone to selection, performance, and expectation bias, as most included trials are unblinded. Finally, the clinical significance of these statistical results has yet to be proved.

The main disadvantages are the more difficult maneuvering technique of the Harmonic scalpel, and cost. An appropriate training program may be implemented to overcome the first disadvantage. Cost, however, remains the main universal issue with the current ultrasonic devices and is presently outweighing potential clinical benefits (if any), and certainly this requires further cost-benefit analysis.

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