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# Single-Incision Laparoscopic Cholecystectomy Versus Traditional Laparoscopic Cholecystectomy: A updated Meta-analysis of Randomized Controlled Trials

**Weizhong Tang[1*], Bo Zhao[2], Xiaoyong Cai2, Yu Lei[2], Jianjun Li[2], Yansong Xu[1], Yubin Huang[2], Fei Huang[2], Wenqi Lu[2], Wenshu Jiang[2], Xiaojian Jin[2]**

[1]Department of Anal and Colorectal Surgery, The First Affiliated Hospital of Guangxi Medical University, Guangxi, China

[2]Department of general Surgery, the Second Affiliated Hospital of Guangxi Medical University, Guangxi, China

[*]**Corresponding author:** Weizhong Tang, Department of Colorectal Surgery, Hospital of Guangxi Medical University, 6 Shuangyong Road, Nanning 530021, China. Tel: +867715322120; Email: tangweizhong6985@163.com.cn

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## Abstract

**Objectives:** To assess the clinical efficacy of Single-Incision Laparoscopic Cholecystectomy (LESS) compared with Traditional Laparoscopic Cholecystectomy (TLC) based on published literature.

**Subjects and Methods:** An online systematic search Randomized Controlled Trials (RCTs) comparing LESS with TLC were included Pubmed, Embase and the Cochrane Library. The inclusion and extraction of the data were completed by two authors independently. Meta-analysis was performed using version Review Manager 5.1.4 software. The clinical outcomes measures were demographics, postoperative Visual Analog Scale pain score, operative complication rate, intraoperative blood loss, cosmetic score, postoperative hospital stay, operating time, wound length; operating time, quality of life score was evaluated by Odds Ratio (OR) and Standard Mean Difference (SMD) according to the different types of data. A meta-analysis of the outcomes was conducted.

**Results:** Fifteen RCTs involving 1069 patients met the predefined inclusion criteria. The cosmetic score of the LESS group was statistically higher than that for TLC. (SMD, 0.55; 95 % CI, 0.20, 0.90; $p = 0.002$); the postoperative hospital stay of the LESS group was statistically shorter than that for TLC. (SMD, -0.24; 95 % CI, -0.44, -0.04; $p = 0.02$); the operating time of LESS groups was statistically longer than TLC. (SMD, 0.83; 95 % CI, 0.52, 1.14; $p < 0.00001$); the wound length of LESS was statistically smaller than TLC. (SMD, -2.90; 95 % CI, - 4.22, -1.58; $p < 0.0001$); the quality of life of LESS was statistically better than that for TLC. (SMD, 1.17; 95 % CI, 0.06, 2.28; $p =0.04$); There was no significant difference between the two groups with Visual Analog Scale pain score, intraoperative blood loss, perioperative complication rate.

**Conclusion:** LESS is associated with a higher cosmetic score, shorter postoperative hospital stays, smaller wound length, better short-term quality of life compared with TLC.

**Keywords:** Laparoscopic Cholecystectomy; Meta-Analysis; Single-Incision; Traditional Laparoscopic Cholecystectomy

## Introduction

Since its introduction in 1980s, the traditional Laparoscopic Cholecystectomy (TLC) through four ports has its advanced to remove the gallbladder for benign pathology by Keus F [1], it has become the gold standard procedure for benign pathology of gallbladder excision. The TLC has less traumatic and cosmetically superior and shorter hospital stay compared with open cholecystectomy [2-4]. In recent years, many new operative techniques were introduced to reduce operative trauma and a nearly scarless lessen postoperative pain, but it did not gain much popularity. Natural Orifice Transluminal Endoscopic Surgery (NOTES) has been introduced for gallbladder surgery; however, its widespread use is very challenging technique and restricted by the limitations of the current technology [5,6]. The Laparoendoscopic Single-Site (LESS) cholecystectomy was introduced to remove the gallbladder, who attempted to complete cholecystectomy through a single port from umbilicus achieve the same objective that was first reported by Navarra [7]. This approach can be executed with refinements of existing technology, such as instrumentation that allows greater articulation and rotation and new retraction systems [8]. The approach is considered a viable minimally invasive procedure that treats benign gallbladder disorders

Many studies have evaluated the feasibility, safety, and efficacy of LESS and TLC. Nevertheless, there are disagreements about the clinical significance between the two surgical procedures. So, we conducted this review was to analyze systematically the Randomized Controlled Trials (RCTs) that compare LESS to TCL to evaluate the comparative effectiveness of LESS and TLC surgery in terms of Visual Analog Scale pain score, intraoperative blood loss, perioperative complication rate, cosmetic score, postoperative hospital stays, operating time, wound length and Quality of life, in patients undergoing cholecystectomy.

## Methods

### Literature Search

The systematic review was conducted according to the Cochrane review guidelines. We searched the data from Pubmed (1990 to February 2014), Embasebz (1990 to February 2014) and the Cochrane Library, Web of Science using the following terms: laparoscopic cholecystectomy, traditional laparoscopic cholecystectomy single-site, single port, single incision, single access, three ports laparoscopic cholecystectomy, four ports laparoscopic cholecystectomy. In addition, a full manual search from the list of each relevant article was also conducted. The studies limits were languages with English and types of RCTs or controlled clinical trial. The searching strategy is shown in (Table 1).

| Reference (year) | Design type | Patients (n) | | Age (years) | | Gender (M/F) | | Journal | Comparison | Measured outcomes |
|---|---|---|---|---|---|---|---|---|---|---|
| | | LESS | TL | LESS | TL | LESS | TL | | | |
| Lai, et al. (2011) [9] | RCT | 27 | 24 | 54.3±12.0 | 51.7±13.3 | 16/8 | 16/11 | The American Journal of Surgery | Four-port TL VS. LESS | 1, 3, 4, 5,7 |
| Ostlie, et al. (2012) [10] | RCT | 30 | 30 | 13.3±3.3 | 14.0±3.2 | 24/6 | 24/6 | Journal of Pediatric Surgery | Four-port TL VS. LESS | 1,5,6,8 |
| Aprea, et al. (2010) [11] | RCT | 25 | 25 | 44.0±10.0 | 45.5± 9.4 | - | - | Journal of Surgical Research | Four-port TL VS. LESS | 1,4,5,6 |
| Evangelos, et al. (2010) [12] | RCT | 20 | 20 | 47.9± 9.8 | 49.2±16.9 | 13/12 | 19/6 | Surg Endosc | Four-port TL VS. LESS | 1,2,3 |
| Phillips, et al. (2012) [13] | RCT | 117 | 80 | 45.6 | 44.1 | 28/29 | 23/56 | Surg Endosc | Four-port TL VS. LESS | 1,2,4,6 |
| Madureira, et al. (2013) [14] | RCT | 28 | 29 | 50 | 56 | 28/89 | 23/56 | Surg Endosc | Four-port TL VS. LESS | 1,2,6,7 |
| Renato, et al. (2013) [15] | RCT | 20 | 20 | - | - | - | - | Surg Endosc | Four-port TL VS. LESS | 1,6 |
| Jun, et al. (2011) [16] | RCT | 21 | 22 | 57.3±16.0 | 45.8±11.9 | - | - | Annals of Surgery | Four-port TL VS. LESS | 1,2,4,6 |
| Saad, et al. (2012) [17] | RCT | 35 | 35 | 49±14 | 45±17 | 26/9 | 28/7 | British Journal of Surgery | Four-port TL VS. LESS | 2,4,5,6 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Sasaki, et al. (2012) [18] | RCT | 27 | 27 | 56.6 (14.2) | /58.2 (12.3) | 14/13 | 14/13 | Surg Laparosc Endosc Percutan Tech | Four-port TL VS. LESS | 1,2,3,4,5,6 |
| Zhan Guo Cao, et al. (2011) [19] | RCT | 57 | 51 | 62.2±5.1 | 59.7±4.4 | 23/34 | 21/29 | Surg Laparosc Endosc Percutan Tech | Four-port TL VS. LESS | 1,2,3,5,6,7 |
| Bucher, et al. (2011) [20] | RCT | 75 | 75 | 42 | 44 | - | - | British Journal of Surgery Society | Four-port TL VS. LESS | 1,2,4,5,6,8 |
| Asakuma, et al. (2011) [21] | RCT | 24 | 25 | 57 | 66 | 11/13 | 13/12 | British Journal of Surgery | Four-port TL VS. LESS | 1,5,6 |
| Mingwei-Zheng, et al. (2012) [22] | RCT | 30 | 30 | 43.6± 11.3 | 46.8± 14.4 | 13/17 | 16/14 | Informa Health-care | Four-port TL VS. LESS | 1,4,6 |
| Lirici, et al. (2011) [23] | RCT | 20 | 20 | - | - | - | - | The American Journal of Surgery | Four-port TL VS. LESS | 1,6 |

**Table 1:** Baseline Characteristics of Studies Included.

The search was conducted on May 2, 2014.

## Inclusion Criteria

All available relevant studies conform to the following criteria: (1) study design was RCTs; (2) Studies that analyzed both LESS and TLC for cholecystectomy; (3) either the higher-quality or the latest article was included when two studies were conducted by the same authors or institution; (4) reporting at least one of the outcomes mentioned below.

## Exclusion criteria

All available relevant studies conform to the following criteria; (1) comparative trials or non-RCTs, Editorials, letters to the editor, review articles, case reports were excluded; (2) studies published repeatedly by different journals; (3) patients with other surgery besides cholecystectomy synchronously; (4) patients with upper abdominal surgery previously.

## Outcomes Measured

All authors agreed to analyze systematically all relevant variables, such as Visual Analog Scale pain score, intraoperative blood loss, perioperative complication rate, cosmetic score, postoperative hospital stay, operating time, wound length and Quality of life score.

## Data Extraction and Quality Assessment

Data extraction and quality assessment were conducted independently by two authors. Disagreements between the authors were settled by accordance. The quality of the RCTs was assessed using the scoring system of Jadad [24] et al, by the two authors. According to this scale, low-quality studies had a score of<2 and high-quality studies had a score of >3 [25]. All outcomes were integrated the software package RevMan 5.1.4 [26], provided by the Cochrane Collaboration, was used for the statistical analysis. We went through all outcomes for clinical and statistical heterogeneity and heterogeneity was determined by chi-squared test. A P value of 0.05 was considered as indicating a significant difference, and I2 values were used for the evaluation of statistical heterogeneity with an I2 of 50% or more indicating presence of heterogeneity [27]. The results were analyzed with the random effect method if significant heterogeneity (P <0.05 was used to define statistically significant heterogeneity). If not, a fixed-effect model was adopted. The odds ratio and the standard mean difference were calculated for dichotomous data and continuous data, respectively. The forest plot was used to show outcome parameters, but the funnel plot was not used to evaluate publication bias because of the small number of studies.

Measured outcomes: 1, Visual Analog Scale pain score 2, operative complication rate 3, intraoperative blood loss 4, cosmetic score 5, postoperative hospital stays 6, operating time 7, wound length 8, quality of life score. F, female; LESS: Laparoendoscopic Single-Site; M, male; RCT: Randomized Controlled Trial; TLC: Traditional Laparoscopic (Table 2).

| Reference (year) | Randomization | Blinding | Withdrawals and dropouts | Jadad score | Setting |
|---|---|---|---|---|---|
| Lai, et al. (2011) [9] | Yes | Double-blind | Clearly reported | 4 | Single center |
| Aprea, et al. (2010) [11] | Yes | Single-blind | Clearly reported | 4 | Single center |
| Evangelos, et al. (2010) [12] | Yes | Single-blind | Clearly reported | 4 | Single center |
| Phillips, et al. (2012) [13] | Yes | Single-blind | Clearly reported | 4 | Multicenter |
| Madureira, et al. (2013) [14] | Yes | Single-blind | Clearly reported | 4 | Single center |
| Renato, et al. (2013) [15] | Yes | Single-blind | Clearly reported | 4 | Single center |
| Jun, et al. (2011) [16] | Yes | Double-blind | Clearly reported | 4 | Single center |
| Saad, et al. (2012) [17] | Yes | Double-blind | Clearly reported | 4 | Single center |
| Sasaki, et al. (2012) [18] | Yes | Double-blind | Clearly reported | 4 | Single center |
| Zhan Guo Cao, et al. (2011) [19] | Yes | Double-blind | Clearly reported | 4 | Single center |
| Bucher, et al. (2011) [20] | Yes | Not stated | Clearly reported | 3 | Single center |
| Mingwei Zheng, et al. (2012) [22] | Yes | Double-blind | Clearly reported | 4 | Single center |
| Lirici, et al. (2011) [23] | Yes | Single-blind | Clearly reported | 4 | Multicenter |
| Asakuma, et al. (2011) [21] | Yes | Single-blind | Clearly reported | 4 | Single center |
| Daniel J. Ostlie, et al. (2012) [10] | Yes | Single-blind | Clearly reported | 4 | Single center |

**Table 2:** Quality Assessment of Studies Included.

Quality assessment using the scoring system of Jadad, et al.

## Results

We found fifteen RCTs that compared LESS with TLC through our database searches. We performed a Meta-analysis of these fifteen RCTs using the data obtained from 1069 patients (556 with LESS and 513 with TLC). The characteristics and methodological quality assessments of the included trials are listed in Tables 1 and 2, respectively.

### Visual Analog Scale pain score

We qualitatively assessed abdominal pain on postoperative at 6-24 hours by means of a VAS. Only 8 trials offered the specific data. The authors managed to extract the matching data for pain scores from 6 to 24 h postoperatively in all included trials. There was significant heterogeneity among the trials (Tau2= 0.30; Chi2 = 34.60, df = 7; p<0.0001; I2 = 80%).In the random-effects model (SMD, -0.02; 95 % CI, -0.45, 0.40; z = 0.11; p = 0.91) (Figure 1).

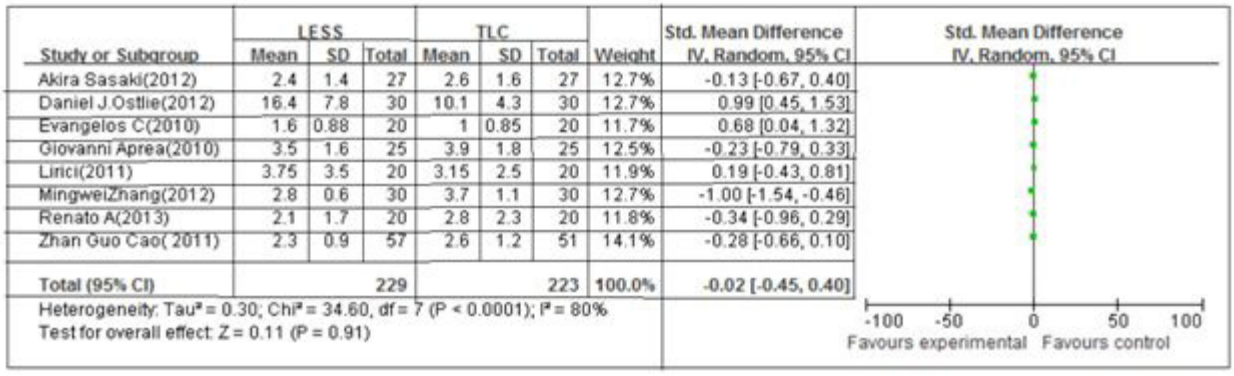


**Figure 1:** Meta-analysis of Visual Analog Scale pain score in Laparoendoscopic Single-Site (LESS) cholecystectomy versus Traditional Laparoscopic Cholecystectomy (TLC) patients. CI, confidence interval; SD, Standard Deviation; IV: Inverse Variance.

The postoperative pain score within 6-24 h was statistically similar for the LESS and TLC patients.

## Perioperative complication rate

Nine trials contributed to the combined calculation of the postoperative complications variable. There Was no heterogeneity among the trials ($Chi^2$= 11.13, df = 8; p=0.19; I2 = 28%).In the M-H, fixed model (OR, 1.01; 95 % CI, 0.61, 1.68; z = 0.05; p = 0.96) (Figure 2).

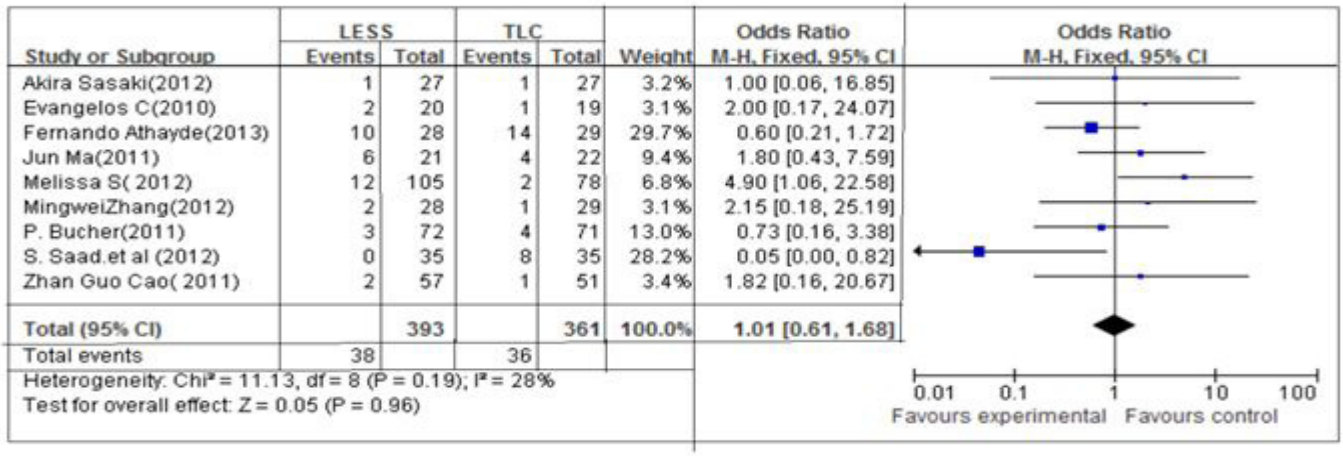


**Figure 2:** Meta-analysis of perioperative complication rate in LESS versus TLC patients.

The perioperative complication rate was statistically similar for both groups.

## Intraoperative Blood Loss

Three trials reported on the intraoperative blood loss, Meta-analysis of the three trials showed no significant difference in the intraoperative blood loss between the two groups ($Tau^2$= 0.22; $Chi^2$ = 8.41, df = 2; p=0.01; $I^2$ = 76%).In the random-effects model (SMD, -0.04; 95 % CI, -0.65, 0.56; z = 0.14; p = 0.89) (Figure 3).

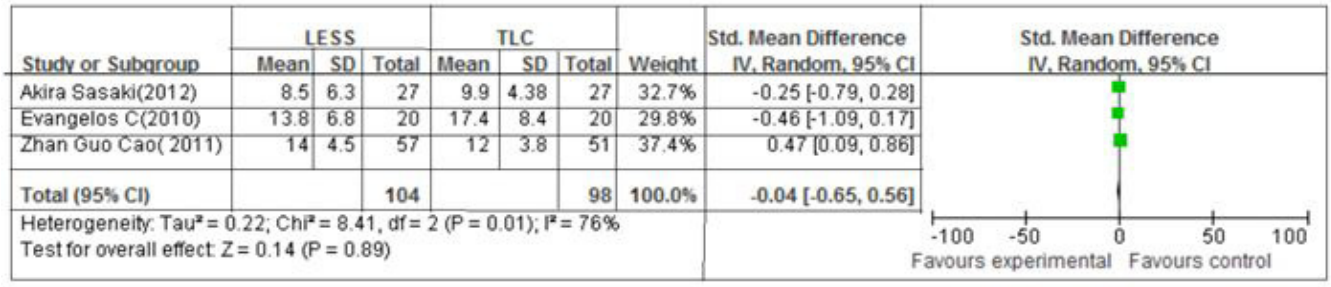


**Figure 3:** Meta-analysis of intraoperative blood loss in LESS versus TLC patients.

The intraoperative blood loss was statistically similar for the LESS and TLC patients.

## Cosmetic score

Six trials contributed to the cosmetic score variable, Meta-analysis of the six trials showed have significant difference in the cosmetic score among the trials ($Tau^2$= 0.10; $Chi^2$ = 10.70, df =4; p=0.03; $I^2$ = 63%).In the random-effects model (SMD, 0.55; 95 % CI, 0.20, 0.90; z = 3.11; p = 0.002) (Figure 4).

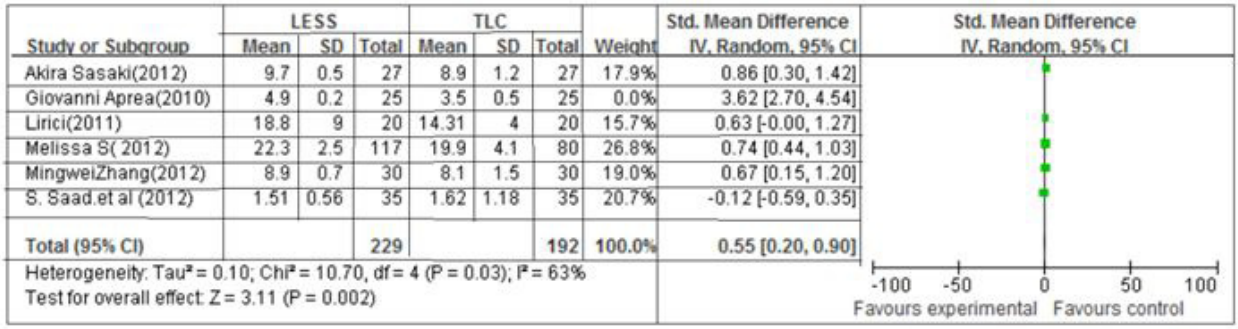


**Figure 4:** Meta-analysis of cosmetic score in LESS versus TLC patients.

The cosmetic score was statistically higher than that for TLC.

## Postoperative Hospital Stay

Six trials contributed to the postoperative hospital stay, Meta-analysis of the six trials showed have significant difference in the postoperative hospital stay among the trials ($Chi^2$ = 10.80, df =5; p=0.06; $I^2$ = 54%).In the fixed-effects model (SMD, -0.24; 95 % CI, -0.44, -0.04; z = 2.35; p = 0.02) (Figure 5).

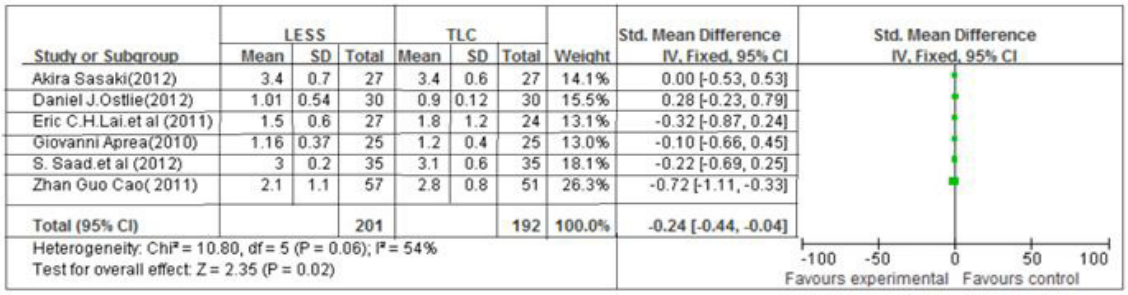


**Figure 5:** Meta-analysis of postoperative hospital stay in LESS versus TLC patients.

The postoperative hospital stay was statistically shorter than that for TLC.

## Operating Time

seven trials contributed to calculate the operating time variable, Meta-analysis of the seven trials showed have significant difference in the operating time among the trials ($Tau^2$ =0.10, $Chi^2$ = 14.38, df =6; p=0.03; $I^2$ = 58%).In the Random-effects model (SMD, 0.83; 95 % CI, 0.52, 1.14; z = 5.25; p < 0.00001) (Figure 6).

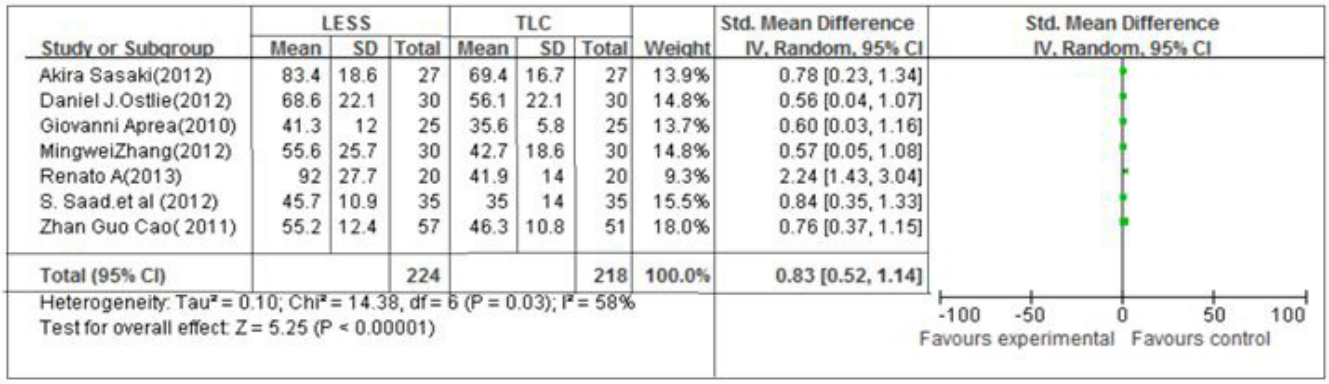


**Figure 6:** Meta-analysis of operating time in LESS versus TLC patients.

The operating time was statistically longer than that for TLC.

### Wound length

two trials contributed to calculate the wound length of abdomen variable, Meta-analysis of the two trials showed have significant difference in the wound length of abdomen between the trials ($Tau^2$ =0.77, $Chi^2$ = 6.50, df =1; p=0.01; $I^2$ = 85%).In the Random-effects model (SMD, -2.90; 95 % CI, - 4.22, -1.58; z = 4.30; p < 0.0001) (Figure 7).

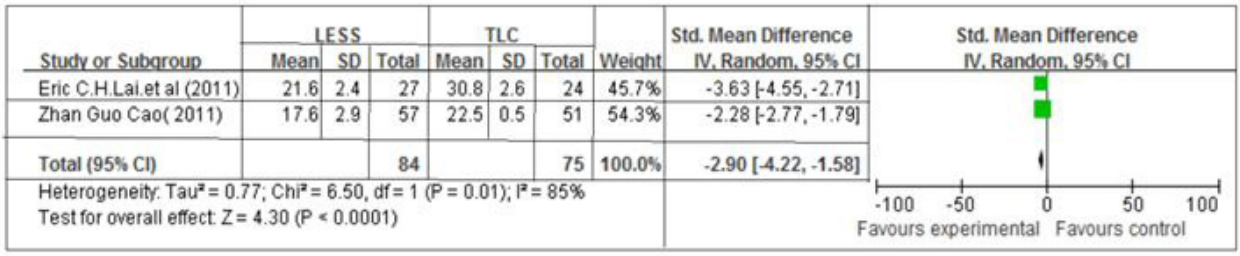


**Figure 7:** Meta-analysis of wound length in LESS versus TLC patients.

The wound length of abdomen was statistically smaller than that for TLC.

### Quality of life

The Quality of life parameter using short forms SF-8 and SF-12 measures the extent to which emotional problems interfere with work or other daily activities. It would be that when there are no visible scars on abdomen, patients' emotions interfere less with work or daily activities [23]. The data of Quality of life variable was extracted between 10 days and 1month after surgery. three trials contributed to calculate the quality of life variable, Meta-analysis of the two trials showed have significant difference in the quality of life among the trials ($Tau^2$ =0.87, $Chi^2$ = 27.88, df =2; p<0.00001; $I^2$ = 93%).In the Random-effects model (SMD, 1.17; 95 % CI, 0.06, 2.28; z = 2.07; p =0.04) (Figure 8).

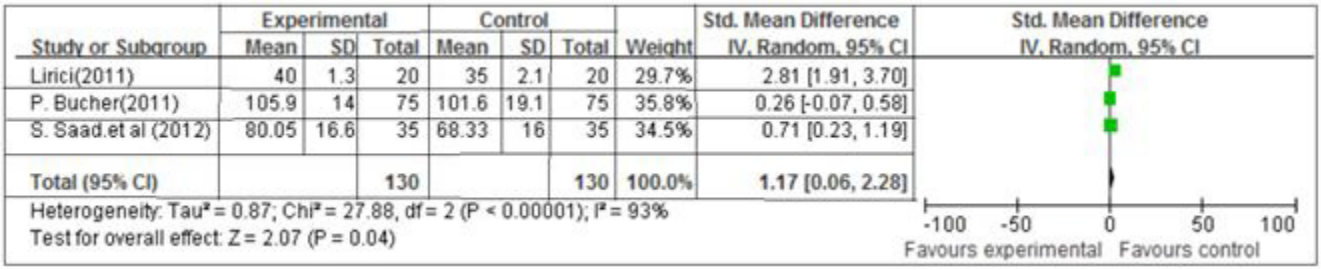


**Figure 8:** Meta-analysis of QoF in LESS versus TLC patients.

The quality of life was statistically better than that for TLC.

## Discussion

This systematic review demonstrates that Visual Analog Scale pain score, intraoperative blood loss, perioperative complication rate, cosmetic score, and postoperative hospital stay, operating time, wound lenth and Quality of life score between LESS and TLC. The literature have shown that TLC compared with open cholecystectomy results in less operative trauma, fewer complication, better recovery, and better cosmetics [28]. In recent years, investigators seeking for better clinical efficacy and cosmetic results, which have attempted to reduce operative trauma further, thus mini-instruments is a step in the direction [29]. While the LESS reduced number of ports and improved the cosmetic results is thought to apply in the benign gallbladder disorders. In the meta-analysis, we attempted to compare the clinical outcomes and advantages of LESS with TLC to shown the superiority of LESS. It involves fifteen RCTs that compared the clinical outcomes for the two procedures for benign gallbladder disorders. Quality assessment by the Jadad score indicated that all literature was of reasonable methodological and high quality and the meta-analysis could offer reliable assessment.

Cosmetic score is statistically advantage of LESS. The approach may be due to the umbilical scar is nearly invisible after surgery, and LESS reduced the number of ports on the abdomen lead to lesser scar after surgery. It may be a driving force espe-

cially for the younger people. The postoperative hospital stay of the LESS group was statistically shorter than that for TLC. The study had shown that LESS resulting in shorter recovery than TLC cholecystectomy [24]. Due to shorter recovery, it may be reducing the postoperative hospital stay. Although, one literatures indicated that there was no statistical significance compare the hospital stay [19], in short words, we comprehensive assessment above review find that LESS could be short the hospital stay. The operating time of the LESS group was statistically longer than TLC. It could be due to the inexperience of the surgeons with the new technique. With increased experience, the mean operating time would be shorter.

The wound length of LESS was statistically smaller than TLC. The average wound length of four ports and three ports cholecystectomy longer than LESS, due to the wound scar of LESS located in the umbilical scar that is nearly invisible after surgery. More and more patients pursue to beauty, thus the approach of LESS seems more popular by patients, especially young women. The quality of life of LESS was statistically better than that for TLC. Because LESS was thought to have better cosmetic outcomes of patient's satisfaction with scars, it may be having a smaller impact on body image and was associated with better quality of life score. In addition, the wound usually hidden single scar in the umbilicus and shorter total scar length, these cosmetic issues may have a favorable influence on quality of life.

In this systematic review, there is no significant difference in Visual Analog Scale pain score, intraoperative blood loss, perioperative complication rate was similar between the LESS and TLC groups. Nevertheless, the research indicates that the LESS is associated with a higher cosmetic score and better quality of life.

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