The Efficacy and Safety of Different Kinds of Laparoscopic Cholecystectomy: A Network Meta Analysis of 43 Randomized Controlled Trials

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Abstract

Background and Objective: We conducted a network meta analysis (NMA) to compare different kinds of laparoscopic cholecystectomy [LC] (single port [SPLC], two ports [2PLC], three ports [3PLC], and four ports laparoscopic cholecystectomy [4PLC], and four ports mini-laparoscopic cholecystectomy [mini-4PLC]).

Methods: PubMed, the Cochrane library, EMBASE, and ISI Web of Knowledge were searched to find randomized controlled trials [RCTs]. Direct pair-wise meta analysis (DMA), indirect treatment comparison meta analysis (ITC) and NMA were conducted to compare different kinds of LC.

Results: We included 43 RCTs. The risk of bias of included studies was high. DMA showed that SPLC was associated with more postoperative complications, longer operative time, and higher cosmetic score than 4PLC, longer operative time and higher cosmetic score than 3PLC, more postoperative complications than mini-4PLC. Mini-4PLC was associated with longer operative time than 4PLC. ITC showed that 3PLC was associated with shorter operative time than mini-4PLC, and lower postoperative pain level than 2PLC. 2PLC was associated with fewer postoperative complications and longer hospital stay than SPLC. NMA showed that SPLC was associated with more postoperative complications than mini-4PLC, and longer operative time than 4PLC.

Conclusion: The rank probability plot suggested 4PLC might be the worst due to the highest level of postoperative pain, longest hospital stay, and lowest level of cosmetic score. The best one might be mini-4PLC because of highest level of cosmetic score, and fewest postoperative complications, or SPLC because of lowest level of postoperative pain and shortest hospital stay. But more studies are needed to determine which will be better between mini-4PLC and SPLC.

Background

Laparoscopic cholecystectomy (LC) has been considered the golden standard for cholecystectomy to manage benign gallbladder disease since 1986 [1-3]. Usually, the standard LC is done using four trocars [3]. These include one port for the camera; one port for instruments used to carry out the dissection, diathermy, clip application; and two ports for manipulation of the gallbladder for adequate exposure of the field of surgery [4]. The fourth (lateral) trocar is used to grasp the fundus of the gallbladder so as to expose Calot’s triangle [3,5]. With increasing surgeon experience, it was argued that the fourth trocar may not be necessary, and LC can be performed safely without using it [3,5]. As a result, three ports laparoscopic cholecystectomy (3PLC) was developed [6,7]. It was thought that reduced size, smaller incision, and fewer ports for LC will improve cosmetic results, decrease pain, and minimize postoperative complications [8,9]. So a trend toward even more minimally invasive approaches, such as smaller ports, mini-ports, and reduced ports, has led to the advent of laparoscopic surgery and its continuous development of laparoscopic surgery [10]. Until 1997, Navarra et al. [11] described the first single port laparoscopic cholecystectomy (SPLC), the LC underwent four stages: four ports (4PLC), three ports (3PLC), two ports (2PLC) and single port (SPLC) according to reduced ports. Then a mini-laparoscopic cholecystectomy (mini-PLC) with smaller ports and incisions was also developed. It was said that SPLC represents the next step in laparoscopic surgery in further reducing the invasiveness of surgical procedures with cosmetic advantages [12]. Although current guidelines recommend performing cholecystectomy via laparoscopy [13], we were not sure what kinds of LC will be the golden standard with minimizing morbidity, decreasing pain and improving cosmetic results. So we conducted a network meta analysis [NMA] to compare different kinds of LC (SPLC, 2PLC, 3PLC, 4PLC, and four ports mini-laparoscopic cholecystectomy (mini-4PLC)).
Methods

We did this systematic review of the available literature in accordance with the PRISMA guidelines [14] for the conduct of meta-analyses of intervention trials.

Data sources

PubMed, the Cochrane library, EMBASE, and ISI Web of Knowledge were searched to find randomized controlled trials (RCTs) and meta analysis using laparoscopic cholecystectomy. Medical Subject Headings terms were also added in all searches for PubMed, Embase, and the Cochrane Library. Reference lists from the meta-analysis, review articles about this topic and identified trials were hand-searched to identify further relevant citations. The search strategy was developed by two reviewers (Lun Li and Jinhui Tian who is a professional searcher over ten years’ experience) and peer-reviewed by a third reviewer (Kehu Yang). And the searches were conducted independently by two reviewers (Lun Li and Jinhui Tian) using the same search strategy to avoid the potential mistakes by anyone of them. The search was conducted in August 2013 without language, date, and publication status restrictions; differences were checked by each other and resolved by discussion. The search was updated in 2013, 1st December.

Inclusion criteria and study selection

The study type should be RCT which used randomized methods according to what they reported. Those studies which used quasi-randomized methods according to what they reported were excluded. The studies should compare two or three surgery instruments (SPLC, 2PLC, 3PLC, 4PLC, and mini-4PLC). SPLC was defined as laparoscopic excision of the gallbladder performed through a single abdominal incision using either a multiport device or different individual ports through the same single skin incision [15]. For 2PLC, 3PLC, and 4PLC, the instruments should be at least 5 mm. For mini-4PLC, two to three of the four instruments should be at least less than 5 mm. Only published articles in English were included, meeting abstracts, and unpublished data were not included in this NMA.

Two independent reviewers (Lun Li and Hongliang Tian) selected the retrieved citations based on titles and abstracts, and full-texts of potential eligible studies were read to decide whether to include based on inclusion criteria. Disagreements were resolved by discussion, and if not, a third reviewer (Kehu Yang) was involved.

Data abstraction and quality assessment

Data was entered into an Excel database by two authors (Lun Li and Jinhui Tian). The following fields were abstracted: country, patient characteristics (age, sex and other baseline characteristics), disease, follow-up duration, and outcomes. Outcomes were extracted preferentially by intention to treat method. Any disagreements were resolved by discussion, and if not, a third reviewer (Kehu Yang) and resolved differences by a third reviewer (Kehu Yang). The following reviewers (Lun Li and Rao Sun) using the same search strategy to arrive at a single, integrated, estimate of the effect of all included treatments based on all included studies. NMA was conducted using ADDIS software. We also produced the rank probability plot by ADDIS software to show which LC was the best. The data was expressed as odds ratio (OR) or MD with 95% Credibility Interval (CrI).

For inconsistency, we undertook a node-splitting analysis by ADDIS software to assess whether direct and indirect evidence on the split node is in agreement [17]. Meanwhile, the methods described by Song [18] were also used to test the difference between DMA or ITC and NMA evidence. A Z value was calculated to show the difference. If the absolute value of Z was more than 1.645, we thought the p value for Z test was less than 0.05. It is deemed significant when p was less than 0.05 or I-square was more than 50%.

Results

Search results

We got 7644 citations from databases and 89 citations from reference checking. Finally we included 43 RCTs [3–7, 19–58]. The searching results and selection process was presented in Figure 1.

Characteristics of included studies

Six studies [20, 27, 44, 46, 56, 58] compared SPLC with 3PLC, two studies [24, 45] compared 2PLC with 4PLC, five studies [5–7, 28, 50] compared 3PLC with 4PLC, 18 studies [25, 29, 34, 35, 37–41, 43, 47, 49, 52–55, 58] compared SPLC with 4PLC, 15 studies [19, 21–23, 30–33, 42, 47, 48, 50, 51, 57] compared 4PLC with mini-4PLC. LC in all included studies was elective, although some studies included patients with acute cholecystitis. And other characteristics of included studies were presented in Table 1.
Quality assessment results

All studies mentioned randomization, but only 13 studies reported the details of the randomized methods and 17 studies mentioned the details of concealed allocations. 11 studies mentioned the methods of blinding, however, patients and assessors were blinded in five studies, patients were blinded in three studies, assessors were blinded in two studies and surgeons were blinded in one study. (Table 2).

Direct pair-wise meta analysis (DMA)

According to the results of DMA, we could see that SPLC was associated with more postoperative complications and higher cosmetic score than 4PLC, longer operative time and higher cosmetic score than 3PLC, more postoperative complications than mini-4PLC. Mini-4PLC was associated with longer operative time than 4PLC. No significantly statistical differences were found in other outcomes between different comparisons. (Table 3, Table 4, Table 5).

Indirect comparison (ITC) and network meta analysis (NMA)

According to the results of ITC, 3PLC was associated with shorter operative time than mini-4PLC and lower postoperative pain level than 2PLC. 2PLC was associated with fewer postoperative complication and longer hospital stay than SPLC. The NMA showed that SPLC was associated with more postoperative complications than mini-4PLC, and longer operative time than 4PLC. (Table 3, Table 4, Table 5).

Inconsistency between DMA/ITC and NMA, heterogeneity for DMA

Node-splitting analysis (Table S1) did not detect any inconsistency among DMA, ITC and NMA except postoperative complications between mini-4PLC and SPLC. Node-splitting analysis showed that there might be inconsistency for postoperative complications (p = 0.01) among DMA, ITC and NMA. Z test did not find any inconsistency DMA/ITC and NMA (Table S2). Even so, high heterogeneity existed for most outcomes in DMA (Table S3).

Rank probability

From the rank probability plot (Table 6), we could see that mini-4PLC has the highest level of cosmetic score, fewest postoperative complications, and lowest amount of intra-operative blood loss. 4PLC has the highest level of postoperative pain, most patients who needed additional analgesics, longest hospital stay, and lowest level of cosmetic score. SPLC has the most post-operative complications, highest amount of intra-operative blood loss, longest operative time, lowest level of postoperative pain, fewest patients who needed additional analgesics and shortest hospital stay. 2PLC has shortest operative time.

Discussion

Summary of finding

Although DMA showed some statistical differences between different groups regarding to the outcomes we focused on, the NMA did not find any significant statistical differences except postoperative complications. However, evidence for this outcome from NMA was not consistent between DMA, ITC and NMA by node-splitting analysis. The rank probability plot suggested 4PLC might be the worst one due to the highest level of postoperative pain, most patients who needed additional analgesics, longest hospital stay, and lowest level of cosmetic score. The best one might be mini-4PLC because of highest level of cosmetic score, fewest postoperative complications, and lowest amount of intra-operative blood loss or SPLC because of lowest level of postoperative pain, fewest patients who needed additional analgesics and shortest hospital stay. However, SPLC has most post-operative complications and highest amount of intra-operative blood loss.

For postoperative pain at the first day, significant differences existed between 3PLC and 4PLC (DMA), 3PLC and 2PLC (ITC). The rank probability showed SPLC might be the best in reducing the first day postoperative pain, and 4PLC might be the worst. Although the inconsistency between DMA or ITC and NMA could not be detected by node-splitting analysis and Z test, the heterogeneity among included studies for direct evidence existed. That might be because of different anesthetics used before surgery and anesthetic prophylaxes after surgery. Due to this point, we did not calculate the amount of anesthetics consumption; we calculated the number of patients who required additional analgesics. And that was why we used the postoperative first day pain level that was measured using VAS at the first postoperative day. This is consistent with the results of the number of patients who required additional analgesics. The rank probability showed that patients in 4PLC group used the most additional analgesics and patients in SPLC group used the fewest additional analgesics, although no significant differences were found in DMA, ITC and NMA.

For postoperative complication, significant differences existed between SPLC and mini-4PLC (DMA), SPLC and 4PLC (DMA and NMA), SPLC and 2PLC (ITC). Rank probability showed that mini-4PLC was associated with fewest postoperative complications, and SPLC was associated with most postoperative complications. Among the included studies, 18 studies reported postoperative complications for SPLC with a median rate of complications being 11.5% (range 10.8% to 12.2%). The evidence from NMA indicated that SPLC might be the best in reducing complications.
**Table 1.** Characteristics of included studies.

| Study     | Country     | I    | C    | Sample size | Gender I:C (F/M) | Age (I:C) | BMI (I:C) |
|-----------|-------------|------|------|-------------|-----------------|-----------|-----------|
| Aprea 2011| Italy SPLC  | 3PLC | 25   | 25          | 13/12:19:6      | 45.5±9.4 | 44.0±10.0 |
| Cao 2011  | China SPLC  | 3PLC | 57   | 51          | 34/23:29:22     | 62.2±5.1 | 59.7±4.4  |
| Pan 2013  | China SPLC  | 3PLC | 49   | 53          | 26/33:21:22     | 43.8±14.0 | 45.2±11.0 |
| Rasic 2010| Croatia SPLC| 3PLC | 48   | 50          | 26/22:32:18     | 44±6.44  | 5.7±6.7   |
| Zheng 2012| China SPLC  | 3PLC | 30   | 30          | 17/13:14:16     | 43.6±11.3 | 43.6±14.4 |
| Brezadola 1999 | Italy 2PLC | 4PLC | 28   | 37          | 19/6:22:15      | 42±20.45 | ±15.15    |
| Poon 2003 | China 2PLC  | 4PLC | 58   | 57          | 33/25:29:28     | 52.3±14.9 | 53.4±13.1 |
| Cerci 2007| Turkey SPLC| 3PLC | 73   | 73          | 54/19:55:18     | 50.08±12.5 | 49.77±13.6 |
| Kumar 2007| Nepal SPLC  | 3PLC | 36   | 39          | 30/6:32:7       | 38.22±13.6 | 67.9±14.10 |
| Trichak 2003| Thailand 3PLC| 4PLC | 100  | 100         | 75/25:73:27     | 53.62±13.1 | 53.74±15.05 |
| Lai 2011  | China SPLC  | 4PLC | 40   | 40          | -               | 45.50    | -         |
| Decarvalho 2013| Brazil mini-4PLC| 4PLC | 23   | 19          | 17/22:18:4      | 45.8±14.9 | 53.4±13.1 |
| Bignell 2013| UK mini-4PLC| 4PLC | 32   | 40          | 28/22:26:4      | 44.42±8.5 | 42.6±9.05 |
| Brown 2013| USA SPLC  | 4PLC | 32   | 39          | 29/11:32:7      | 42±4.3  | 29.4±5.13 | 60.3±6.9 |
| Binner 2013| Switzerland | 4PLC | 24   | 27          | -               | 75.75    | -         |
| Chang 2013| Singapore SPLC | 4PLC | 12   | 12          | 14/10:16:10     | 49.46±11.3 | 39:51:12.3 |
| Lai 2011  | China SPLC  | 4PLC | 24   | 27          | 16/8:16:11      | 51.7±13.3 | 54.3±12.0 |
| Trichak 2003| Thailand 3PLC| 4PLC | 100  | 100         | 75/25:73:27     | 53.62±13.1 | 53.74±15.05 |
| Bresadola 1999 | Italy 2PLC | 4PLC | 20   | 20          | -               | 25.27    | -         |
| Ma 2011   | Portugal SPLC| 4PLC | 21   | 22          | -               | 57.3±16.4 | 58.1±11.9 |
| Madureira 2013| Brazil 4PLC| 28   | 29   | 28          | 14/13:14:13     | 56.6±14.2 | 58.2±12.3 |
| Marks 2013| USA 4PLC   | 119  | 81   | 91/28:57:24 | 45.8:44.0       | 29.30:9  |
| Mehmoood 2010| Pakistan SPLC| 4PLC | 30   | 30          | 28/22:64:4      | 44.42±8.5 | 9.42±9.05 |
| Ostlie 2013| USA SPLC   | 4PLC | 30   | 30          | 24/6:24:6       | 14.0±3.6 | 23:3.3    |
| Saad 2013 | Germany SPLC| 4PLC | 35   | 35/35      | 28/7:29:62/9:6  | 45.49:44 | 25.4±25.4 |
| Sasaki 2012| Japan SPLC  | 4PLC | 27   | 27          | 14/13:14:13     | 56.6±14.2 | 58.2±12.3 |
| Sinan 2012| Turkey SPLC| 4PLC | 17   | 17          | 13/4:9:8        | 48.5±8.9 | 46.7±4.3  |
| Tsimoyiannis 2010 | Greece 4PLC | 17   | 17   | 15:5:19:1   | 49.2±16.94.79:9.8 | 7.3±1.27:2.9 |
| Yilmaz 2013| Turkey SPLC| 4PLC | 43   | 40          | 34/9:27:13      | 48.5±12.0 | 51.0±9.0  |
| Zap 2013  | USA 4PLC   | 49   | 51   | 42/7:34:17  | 44.2±16.2:50.9 | 18.2±2.9 | 14.5±30.0:6.3 |
| Alponat 2002| Turkey mini-4PLC| 4PLC | 17   | 22          | 15/2:18:4       | 45.8±13.3 | 49.7±11.8 |
| Bignell 2013| UK mini-4PLC | 4PLC | 10   | 10          | 29/11:36:4      | 54.52    | -         |
| Bisgaard 2000| Denmark mini-4PLC| 4PLC | 13   | 13          | 13/3:9:4        | 46.53    | 25.26     |
| Bisgaard 2002| Denmark mini-4PLC| 4PLC | 25   | 27          | 22/3:20:7       | 47.48    | 26.27     |
| Cheah 2001| Singapore mini-4PLC| 4PLC | 37   | 38          | 23/4:21:17      | 49.52    | -         |
| Decarvalho 2013| Belgium mini-4PLC| 4PLC | 18   | 23          | 16:21:8:5       | 47±14.2 | 19         |
| Hsieh 2003| China mini-4PLC| 4PLC | 35   | 29          | 19/15:15:14     | 55.7±17.7 | 54.5±17.6 |
| Huang 2003| China mini-4PLC| 4PLC | 54   | 30          | 37/33:18:12     | 49.5±14.8 | 24.7±14.2 |
| Look 2001 | Singapore mini-4PLC| 4PLC | 28   | 36          | 16/12:21:15     | 54.3±12.3 | 51.3±14.4 |
| Novitsky 2005| USA mini-4PLC| 4PLC | 34   | 33          | 29/4:26:8       | 46.7±12.1 | 41.8±12.4 |
| Sari 2003 | Italy mini-4PLC| 4PLC | 67   | 68          | 37:29:34:34     | 53.5±6.6 | 27.3±26.2 |
| Schmidt 2002| Germany mini-4PLC| 4PLC | 20   | 20          | -               | 52.4±15.5 | 54.07±11.9 |
| Schweng 2000| Germany mini-4PLC| 4PLC | 25   | 25          | 18/7:17:8       | 44.52    | 21.7±22.9 |
| Ainslie 2003| UK mini-4PLC | 4PLC | 21   | 19          | -               | 58.49    | 24.5±27.7 |

I: intervention group; C: control group; F: female; M: male.
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6.46% (0%–35.71%), one studies reported postoperative complications for 2PLC (5.17%), five studies reported postoperative complications for 3PLC with a median rate of 3.33% (1.96%–9.43%), 19 studies reported postoperative complications for 4PLC with a median rate of 6.17% (0%–48.28%), five studies reported postoperative complications for mini-4PLC with a median rate of 2.50% (0%–8.57%). However, node-splitting analysis showed there were inconsistencies between mini-4PLC and SPLC, 4PLC and 3PLC, although Z test did not find any inconsistency between DMA/ITC and NMA evidence and there were not high

| Study         | Randomization | Allocation concealed | Blinding | Incomplete data | Selective reporting | Other bias |
|---------------|---------------|---------------------|----------|----------------|---------------------|------------|
| Aprea 2011    | M             | Y                   | N        | N              | U                   | U         |
| Cao 2011      | M             | Y                   | D        | N              | U                   | U         |
| Pan 2013      | Y             | Y                   | U        | U              | U                   | U         |
| Rasic 2010    | Y             | U                   | U        | N              | N                   | U         |
| Zheng 2012    | Y             | Y                   | U        | N              | N                   | U         |
| Bresadola 1999| M             | U                   | U        | N              | N                   | U         |
| Poon 2003     | M             | U                   | M        | U              | U                   | U         |
| Cerci 2007    | M             | U                   | U        | U              | U                   | U         |
| Kumar 2007    | M             | U                   | U        | U              | U                   | U         |
| Trichak 2003  | M             | U                   | U        | U              | U                   | U         |
| Gupta 2005    | M             | U                   | U        | U              | U                   | U         |
| Brown 2013    | M             | U                   | P        | U              | U                   | U         |
| Bucher 2011   | Y             | U                   | U        | N              | N                   | U         |
| Chang 2013    | M             | U                   | D, P     | Y              | N                   | U         |
| Lai 2011      | Y             | Y                   | U        | N              | N                   | U         |
| Lirici 2010   | M             | Y                   | P        | N              | U                   | U         |
| Luna 2013     | M             | U                   | U        | U              | U                   | U         |
| Ma 2011       | M             | U                   | U        | U              | N                   | U         |
| Madureira 2013| M             | U                   | U        | Y              | N                   | U         |
| Marks 2013    | M             | U                   | U        | U              | Y                   | U         |
| Mehmod 2010   | M             | Y                   | U        | U              | N                   | U         |
| Ostlie 2013   | Y             | U                   | U        | U              | U                   | U         |
| Saad 2013     | Y             | Y                   | D, P     | N              | N                   | U         |
| Sasaki 2012   | Y             | U                   | U        | Y              | N                   | U         |
| Sinai 2012    | Y             | U                   | U        | Y              | U                   | U         |
| Tsimoyiannis 2010 | M       | Y                   | U        | N              | N                   | U         |
| Yilmaz 2013   | M             | U                   | U        | U              | U                   | U         |
| Zapf 2013     | Y             | U                   | U        | U              | U                   | U         |
| Alponat 2002  | M             | U                   | U        | U              | U                   | U         |
| Bignell 2013  | M             | U                   | U        | U              | U                   | U         |
| Bilsgaard 2000| M             | Y                   | D, P     | Y              | N                   | U         |
| Bilsgaard 2002| Y             | Y                   | U        | Y              | Y                   | Y         |
| Cheah 2001    | M             | Y                   | U        | U              | U                   | U         |
| Decarvalho 2013| M           | Y                   | U        | N              | N                   | U         |
| Hsieh 2003    | M             | U                   | U        | Y              | Y                   | U         |
| Huang 2003    | M             | Y                   | U        | Y              | N                   | U         |
| Look 2001     | M             | U                   | P        | U              | U                   | U         |
| Nvitsky 2005  | Y             | U                   | D, P     | Y              | Y                   | U         |
| Sarli 2003    | M             | Y                   | D        | Y              | N                   | U         |
| Schmidt 2002  | M             | U                   | S        | N              | Y                   | U         |
| Schwenk 2000  | M             | U                   | U        | U              | Y                   | U         |
| Ainslie 2003  | M             | U                   | U        | Y              | N                   | U         |
| Khorgami 2013 | Y             | Y                   | D, P     | N              | N                   | U         |

M: mentioned; U: unclear; N: no; D: blinded to data collectors; P: blinded to patient; S: blinded to surgeon; Y: yes, adequately reported.
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ADDIS software was used, but similar results were found. Heterogeneity for the direct evidence. So inconsistency model in consistent with the previous probability.

Differences among any two comparisons. And the rank probability showed that mini-4PLC has the best cosmetic scores, and 4PLC showed that mini-4PLC-3PLC *0.33 [–0.06, 0.71] \text{i(p)} –0.01 (–0.40, 0.36) **–0.04 [–0.46, 0.37] \text{i(p)} –0.00 (–0.38, 0.37) 6.41 [3.21, 9.62] \text{i(p)} 3.74 (–8.28, 15.36 )

Table 3. Meta analysis for postoperative pain, additional analgesics and intra-operative blood loss.

|            | Postoperative pain | Pain control | Blood loss |
|------------|-------------------|--------------|------------|
|            | DMA/ITC \text{^d} | NMA \text{^a} | DMA/ITC \text{^d} | NMA \text{^a} | DMA/ITC \text{^d} | NMA \text{^a} |
| mini-4PLC-4PLC | –0.30 [–1.38, 0.78] | d | –0.32 [–1.40, 0.77] | d | 1.00 [0.38, 2.64] | d | 0.83 (0.30, 2.06) | d | –6.37 [–26.97, 14.23] | d | –8.07 (–27.26, 12.67) |
| mini-4PLC-3PLC | 0.29 [–0.86, 1.44] | i(p) | 0.30 [–1.22, 1.92] | i | *0.90 [0.31, 2.59] | i(p) | 0.79 (0.12, 3.86) | i | –5.65 [–26.62, 15.32] | i | –7.21 (–27.14, 13.81) |
| mini-4PLC-2PLC | –0.29 [–1.40, 0.82] | i(p) | –0.13 [–2.48, 2.26] | i | | | | | | |
| mini-4PLC-SPLC | 0.42 [–1.04, 1.88] | i(p) | 0.38 [–0.93, 1.73] | i | 0.84 [0.27, 2.65] | i | 1.51 (0.39, 4.88) | i | –6.22 [–26.98, 14.54] | i | –7.83 (–27.04, 12.78) |
| 4PLC-3PLC | 0.59 [0.20, 0.98] | d | 0.63 [–0.48, 1.73] | d | 1.61 [0.41, 6.67] | d | 0.95 (0.20, 3.99) | d | 0.72 [–3.2 4.64] | d | 0.55 (–4.58, 5.73) |
| 4PLC-2PLC | 0.01 [–0.22, 0.25] | d | 0.20 [–1.97, 2.30] | d | | | | | | |
| 4PLC-SPLC | 0.72 [–0.25, 1.70] | d | 0.70 [–0.07, 1.47] | d | 2 [0.86, 4.55] | d | 1.84 (0.69, 4.68) | d | 0.15 [–2.46,2.75] | d | –0.02 (–2.94, 3.23) |
| 3PLC-2PLC | –0.58 [–1.04, –0.13] | d | –0.42 [–2.85, 1.98] | d | | | | | | |
| 3PLC-SPLC | 0.13 [–0.41, 0.67] | d | 0.07 [–0.96, 1.10] | d | 1.35 [0.69, 2.86] | d | 1.92 (0.56, 7.61) | d | –0.57 [–3.5 2.37] | d | –0.70 (–4.39, 3.66) |
| 2PLC-SPLC | 0.71 [–0.29, 1.71] | d | 0.50 [1.74, 2.80] | d | | | | | | |

d: DMA, direct pair-wise meta analysis; i: ITC, indirect treatment comparison meta analysis; i(4): indirect treatment comparison meta analysis via 4PLC; i(1): indirect treatment comparison meta analysis via SPLC; i(p): pooled results of indirect treatment comparison meta analysis.

For hospital stay, DMA and NMA did not show any significant differences; only ITC showed that 2PLC was associated with longer hospital stay than SPLC. And the rank probability showed that SPLC was associated with shortest hospital stay, and 4PLC was associated with longest hospital stay. Due to some studies used hours to measure the length of hospital stay, we conduct sensitive analysis. Sensitive analysis of DMA, ITC and NMA showed no differences among any two comparisons. And the rank probability of sensitive analysis was consistent with the previous one. As LC has a faster recovery, many hospitals conducted day-surgery rather than overnight stay surgery. And culture and hospital types could also affect the length of hospital stay. And these factors might be the reasons for the heterogeneity of the direct evidence.

Two operative outcomes, operative time and intra-operative blood loss, were evaluated. Significances existed between SPLC and 4PLC, 4PLC and 3PLC, mini-4PLC and 4PLC (DMA), mini-4PLC and 3PLC (ITC), SPLC and 4PLC (NMA) for operative time.
time. The rank probability showed that SPLC was associated with the longest operative time, and 2PLC was associated with the shortest operative time. For intra-operative blood loss, no inconsistencies were found between DMA/ITC and NMA except postoperative complications. Although we used inconsistency model to analyze the data, the results and conclusions did not change.

Strengths and limitations
This is the first ITC and NMA which compared different kinds of LC. We also calculated the inconsistency using node-splitting analysis and Z test. Inconsistency model and sensitive analysis were used to test the stability of the results, and the results did not change for DMA and NMA. However, our NMA has its own limitations: first, our NMA only included studies which specified how many ports they used during their surgery. For those studies that it is hard to judge whether 4PLC or 3PLC, we excluded them. For example, study conducted by Vilallonga [63] did not specify what their standard LC is, so we excluded it. Second: we did not include quasi-randomized studies. For example, we excluded two studies [64,65] as they used quasi-randomized study design. We included lots of studies [30/43] which just mentioned randomization, but they did not report the detail of the randomization. Due to the high risk of bias in most of the studies, the results of our DMA, ITC and NMA might be biased. Third: the heterogeneity for DMA is high. It was said that heterogeneity between the sets of studies that contribute direct comparisons to an indirect comparison or a network meta-analysis would indicate a lack of similarity [66]. We checked the clinical and methodological similarity among all included studies, and then we found indeed there were some differences among all included studies, such as different analgesics used before and after surgery, different instruments during the surgery, studies from different countries, and some variances for the LC. Even so, inconsistency was not found for most outcomes, except postoperative complications. However, the inconsistency model did not change the results. Fourth: there were many factors that might affect length of hospital stay, such as culture differences and hospital types; however, we did not conduct subgroup analysis due to limited data.

Table 5. Meta analysis for postoperative complications and cosmetic score.

| Postoperative complications | DMA/ITC | NMA | Inconsistency | Cosmetic score | Sensitive analysis for cosmetic score |
|-----------------------------|---------|-----|--------------|----------------|--------------------------------------|
|                             |         |     |              | DMA/ITC# | NMA# | DMA/ITC# | NMA# |
| mini-4PLC-4PLC | 0.61 [0.20, 1.86]d | 0.31 [0.05, 1.41] | 0.38 [0.06, 1.90] | 1.60 [-0.05, 3.24]d | 1.50 [-0.11, 3.55] | 2.97 [-1.58, 7.53]d | 1.60 [-0.39, 3.98] |
| mini-4PLC-PLC | *0.14 [0.01, 1.94]p(i) | 0.19 [0.01, 1.89] | 0.09 [0.00, 1.93] | 1.69 [-0.12, 3.50]p(i) | 1.72 [-0.49, 4.25] | 3.06 [-1.56, 7.68]p(i) | 1.80 [-1.01, 5.07] |
| mini-4PLC-3PLC | 1.56 [0.26, 9.22]i | 0.87 [0.03, 19.86] | 1.07 [0.04, 26.67] | 1.2 [-0.56, 2.96]i | 1.11 [-2.20, 4.78] | 2.57 [-2.03, 7.17]i | 1.19 [-2.94, 5.68] |
| mini-4PLC-PLC | 0.05 [0.00, 0.98]d | 0.14 [0.02, 0.77] | 0.04 [0.00, 0.66] | 1.01 [-0.71, 2.73]d | 0.61 [-1.40, 2.97] | 2.47 [-2.14, 7.08]d | 0.82 [-1.86, 3.96] |
| 4PLC-3PLC | 0.32 [0.01, 8.33]d | 0.62 [0.08, 3.41] | 0.25 [0.00, 3.93] | 0.09 [-0.68, 0.05]d | 0.20 [-1.39, 1.72] | 0.09 [-0.68, 0.05]d | 0.20 [-1.90, 2.35] |
| 4PLC-2PLC | 2.56 [0.63, 10]d | 2.72 [0.20, 50.70] | 2.75 [0.20, 46.82] | -0.40 [-1.02, 0.22]d | -0.41 [-3.39, 2.65] | -0.40 [-1.02, 0.22]d | -0.38 [-4.13, 3.23] |
| 4PLC-SPLC | 0.54 [0.34, 0.85]d | 0.46 [0.17, 1.05] | 0.49 [0.18, 1.14] | -0.59 [-1.09, -0.10]d | -0.90 [-2.14, 0.30] | -0.50 [-1.17, 0.18]d | -0.78 [-2.63, 1.17] |
| 4PLC-PLC | 8.21 [0.21, 158.79]i | 12.67 [0.27, 2640.41] | -0.49 [-1.48, 0.50]i | -0.60 [-3.84, 2.91]i | -0.49 [-1.48, 0.50]i | -0.61 [-4.93, 3.54] |
| 3PLC-2PLC | 0.69 [0.27, 1.72]d | 0.75 [0.15, 4.31] | 0.75 [0.17, 4.34] | -1.13 [-0.06, -2.19]d | -1.09 [-2.44, 0.22] | -1.04 [-2.32, 0.23]d | -0.98 [-2.91, 0.95] |
| 3PLC-SPLC | 0.21 [0.05, 0.91]i | 0.17 [0.01, 2.58] | 0.06 [0.00, 2.27] | -0.19 [-0.98, 0.60]i | -0.48 [-3.85, 2.64]i | -0.1 [-1.02, 0.82]i | -0.38 [-4.34, 3.89] |
| 3PLC-PLC | 0.05 [0.00, 0.98]d | 0.14 [0.02, 0.77] | 0.04 [0.00, 0.66] | 1.01 [-0.71, 2.73]d | 0.61 [-1.40, 2.97] | 2.47 [-2.14, 7.08]d | 0.82 [-1.86, 3.96] |

| Mini-4PLC | 0.31 [0.05, 1.41] | 0.17 [0.01, 2.58] | 0.06 [0.00, 2.27] | -0.19 [-0.98, 0.60]i | -0.48 [-3.85, 2.64]i | -0.1 [-1.02, 0.82]i | -0.38 [-4.34, 3.89] |

| d: DMA, direct pair-wise meta analysis; i: ITC, indirect treatment comparison meta analysis; i(4): indirect treatment comparison meta analysis via 4PLC; i(1): indirect treatment comparison meta analysis via SPLC; p(i): pooled results of indirect treatment comparison meta analysis. |

Table 6. Rank probability.

| Drug | Pain | Additional analgesics | Complication | Blood loss | cosmetic score | sensitive analysis | Hospital stay | sensitive analysis | Operative time |
|------|------|-----------------------|--------------|------------|----------------|--------------------|----------------|--------------------|----------------|
| SPLC | 0.31 | 0.64                  | 0.00         | 0.05       | 0.18           | 0.17               | 0.40           | 0.41               | 0.00           |
| 2PLC | 0.24 | 0.45                  |              |            | 0.19           | 0.21               | 0.16           | 0.16               | 0.76           |
| 3PLC | 0.29 | 0.11                  | 0.03         | 0.17       | 0.01           | 0.02               | 0.15           | 0.17               | 0.11           |
| 4PLC | 0.00 | 0.03                  | 0.01         | 0.08       | 0.00           | 0.00               | 0.00           | 0.00               | 0.11           |
| mini-4PLC | 0.15 | 0.21                  | 0.51         | 0.70       | 0.61           | 0.60               | 0.28           | 0.26               | 0.02           |

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Implications to future research and practice

Most included studies did not mention the details of randomization and concealed allocation, nearly all of them were of small sample size. In the future randomized controlled studies of big sample size should be well conducted and adequately reported. For outcomes, such as postoperative pain, hospital stay should be measured using international standards, such as VAS for pain, day for hospital stay. Regarding to cosmetic scores, too many scales were used in the primary studies, which scale will be better to measure the cosmetic satisfaction? This needs a comparative study to test the usability of different scales. Based on our NMA, we could see that 4PLC might be the worst, but it is hard to decide which one is the best, as few studies compared SPLIC with mini-4PLC. The rank probability showed that either SPLIC or mini-4PLC will be the best, although SPLIC has the most post-operative complications, highest amount of intra-operative blood loss, and longest operative time. As a result, future more studies were needed to compare SPLIC with mini-4PLC.

Based on the rank probability, we should make sure to let patients know that SPLIC was associated with lowest postoperative pain, most postoperative complications, and longest hospital stay, mini-4PLC was associated with high level cosmetic score and fewest complications. For surgeons, when conducting SPLIC, please pay attention to the intra-operative blood loss and postoperative complications.

Supporting Information

Table S1 Node-splitting analysis. (DOC)
Table S2 Z test for inconsistency. (DOC)
Table S3 I² test for heterogeneity. (DOC)
Checklist S1 PRISMA checklist. (DOC)

Author Contributions

Conceived and designed the experiments: LL, JT HT QW RS KY. Performed the experiments: LL, JT HT QW RS KY. Analyzed the data: LL, JT KY. Contributed reagents/materials/analysis tools: LL, JT KY. Wrote the paper: LL, JT HT QW RS KY. Entered data into software: LL, JT. Checked the data in the software: KY. Revised manuscript: LL, JT HT QW RS KY.

References

1. Wu XS, Shi LB, Gu J, Dong P, Lu JH, et al. (2013) Single-Incision Laparoscopic Cholecystectomy Versus Multiport Laparoscopic Cholecystectomy: A Meta-analysis of Randomized Clinical Trials. Journal of Laparoendoscopic & Advanced Surgical Techniques 23: 183–191.
2. Puzziello A, Orlando G, Sani C, Gervasi R, Lerose MA, et al. (2012) From 3-Port to New Laparoscopic Single-Site (LESS) Cholecystectomy: A Critical Analysis of Available Evidence. Surgical Innovation 19: 364–369.
3. Sun SL, Yang KH, Gao MT, He XD, Tian JH, et al. (2009) Three-Port Versus Four-Port Laparoscopic Cholecystectomy: Meta-Analysis of Randomized Clinical Trials. World Journal of Surgery 33: 1904–1908.
4. Gurunathan Kuniruchi S, Janmacker S, Davidson Brian R (2008) Two or three ports versus four ports for laparoscopic cholecystectomy. Cochrane Database of Systematic Reviews: John Wiley & Sons, Ltd.
5. Kumar M, Agraval CS, Gupta RK (2007) Three-port versus standard four-port laparoscopic cholecystectomy: a randomized controlled trial in a community-based teaching hospital in eastern Nepal. JSLS : Journal of the Society of Laparoendoscopic Surgeons/Society of Laparoendoscopic Surgeons. pp. 358–362.
6. Gupta A, Shrivastava UK, Kumar P, Burman D (2005) Minilaparoscopic versus laparoscopic cholecystectomy: a randomized controlled trial. Tropical gastroenterology : official journal of the Digestive Diseases Foundation. pp. 149–151.
7. Trichak S (2003) Three-port vs standard four-port laparoscopic cholecystectomy: a prospective randomized study. Surgical Endoscopy, pp. 1434–1436.
8. Garg P, Thakur JD, Garg M, Menon GR (2012) Single-Incision Laparoscopic Cholecystectomy vs Conventional Laparoscopic Cholecystectomy: a Meta-analysis of Randomized Controlled Trials. Journal of Gastrointestinal Surgery 16: 1615–1628.
9. Sharma A, Dalhia P, Khullar R, Soni V, Bajaj M, et al. (2012) Single-Incision Laparoscopic Surgery (SILS) in Biliary and Pancreatic Diseases. Indian Journal of Surgery 74: 13–21.
10. Antoniou SA, Pointner R, Granderrath FA (2011) Single-incision laparoscopic cholecystectomy: a systematic review. Surgical Endoscopy and Other Interventional Techniques 25: 367–372.
11. Arezzo A, Scozzi G, Famiglietti F, Passera R, Morino M (2013) Is single-incision laparoscopic cholecystectomy safe? Results of a systematic review and meta-analysis. Surgical Endoscopy and Other Interventional Techniques 27: 2993–2994.
12. Pucher PH, Sodergren MH, Singh P, Darzi A, Parakseva P (2013) Have we enough to go forward? A systematic review of the randomised controlled trials. Cochrane Database of Systematic Reviews: John Wiley & Sons, Ltd.
13. Qiu JG, Yuan HC, Chen ST, Guo ZL, Han P, et al. (2013) Single-Port Versus Conventional Multiport Laparoscopic Cholecystectomy: A Meta-analysis of Randomized Controlled Trials and Nonrandomized Studies. Journal of Laparoendoscopic & Advanced Surgical Techniques 23: 015–031.
14. Mohler D, Liberveri A, Tezfeldl J, Ahlman DG (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 339:b2535.
15. Trastulli S, Cirocchi R, Desiderio J, Guarino S, Santoro A, et al. (2013) Systematic review and meta-analysis of randomised clinical trials comparing single-incision versus conventional laparoscopic cholecystectomy. British Journal of Surgery 100: 191–208.
16. Higgins JPT, S. G Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration. Available: www.Cochrane-handbook.org.
17. Daw J, Welton NJ, Caldwell DM, Ades AE (2010) Checking consistency in mixed treatment comparison meta-analysis. Stat Med 29: 932–944.
18. Song F, Xiong T, Parekh-Bhurke S, Loke YK, Sutton AJ, et al. (2011) Inconsistency between direct and indirect comparisons of competing interventions: meta-epidemiological study. BMJ 343: e4969.
19. Alponat A, Cambiucci A, Griselli C, Cantu RE, Ozbek O (2002) Is minilaparoscopic cholecystectomy less traumatic? Prospective randomized study comparing minilaparoscopic and conventional laparoscopic cholecystectomies. World Journal of Surgery, pp. 1437–1440.
20. Aprea G, Coppola Bottazzi E, Guida F, Masone S, Persico G (2011) Laparoscopic single site (LESS) versus classic video-laparoscopic cholecystectomy: a randomized prospective study. The Journal of surgical research. pp. e109–112.
21. Biggell M, Cheong E, Lewis MP, Rhodes M (2012) A randomised, single blind study of miniports (3mm) versus conventional ports in laparoscopic cholecystectomy. Gastroenterology 142: S1034.
22. Biauga T, Klarskov B, Trap R, Kehlet H, Rosenberg J (2000) Pain after microlaparoscopic cholecystectomy. A randomized double-blind controlled study. Surgical Endoscopy, pp. 340–344.
23. Biauga T, Klarskov B, Trap R, Kehlet H, Rosenberg J (2002) Microlaparoscopic vs conventional laparoscopic cholecystectomy: a prospective randomized double-blind trial. Surgical Endoscopy, pp. 458–464.
24. Bresadola F, Pasquale AL, Donini A, Chiariandini P, Anania G, et al. (1999) Elective transumbilical comparison with standard laparoscopic cholecystectomy. The European journal of surgery = Acta chirurgica. pp. 29–34.
25. Brown KM, Moore BT, Sorenson GB, Boettger CH, Tang F, et al. (2013) Patient-reported outcomes after single-incision versus traditional laparoscopic cholecystectomy: A randomized prospective trial. Surgical Endoscopy and Other Interventional Techniques 27: 3108–3113.
26. Bocher P, Pagin F, Buch NC, Ostermann S, Morel P (2011) Randomized clinical trial of laparoscopic single-site versus conventional laparoscopic cholecystectomy. British Journal of Surgery 98: 1695–1702.
27. Cao ZG, Cai W, Qin MF, Zhao HZ, Yue P, et al. (2011) Randomized Clinical Trial of Single-incision Versus Conventional Laparoscopic Cholecystectomy: Short-term Operative Outcomes. Surgical Laparoscopy Endoscopy & Percutaneous Techniques 21: 311–313.
28. Cecchi G, Tarhan OR, Barut I, Bulbul M (2007) Three-port versus four-port laparoscopic cholecystectomy. Hepato-Gastroenterology, pp. 15–16.
29. Chang SK, Wang YL, Shen LI, Iyer SG, Shaik AB, et al. (2013) Interim report: a randomized controlled trial comparing postoperative pain in single-incision laparoscopic cholecystectomy and conventional laparoscopic cholecystectomy. Asian J Endosc Surg 6: 14–20.
30. Cheah WK, Lenzi JE, So JB, Kum CK, Goh PM (2001) Randomized trial of needlescopic versus laparoscopic cholecystectomy. The British journal of surgery, pp. 45–47.

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31. de Carvalho LFA, Fierro K, Kint M (2013) Mini-Laparoscopic Versus Conventional Laparoscopic Cholecystectomy: A Randomized Controlled Trial. Journal of Laparoendoscopic & Advanced Surgical Techniques 23: 109–116.

32. Hsieh CH (2005) Early minilaparoscopic cholecystectomy in patients with acute cholecystitis. American Journal of Surgery 185: 344–348.

33. Huang MT, Wang W, Wei PL, Chen RJ, Lee VJ (2003) Minilaparoscopic and laparoscopic cholecystectomy: a comparative study. Archives of surgery (Chicago, Ill : 1960). pp. 1017–1023.

34. Lai ECH, Yang GPC, Tang CN, Yih PCL, Chan OCY, et al. (2011) Prospective randomized comparative study of two incision laparoscopic cholecystectomy versus conventional four-port laparoscopic cholecystectomy. American Journal of Surgery 202: 254–258.

35. Lirici MM, Califfano AD, Angelini P, Corcione F (2011) Laparoscopic single site cholecystectomy versus standard laparoscopic cholecystectomy: results of a pilot randomized trial. American Journal of Surgery 202: 43–52.

36. Look M, Chew SP, Tan YC, Liew SE, Cheong DMX, et al. (2001) Post-operative pain in needleless versus conventional laparoscopic cholecystectomy: A prospective randomised trial. Journal of the Royal College of Surgeons of Edinburgh 46: 138–142.

37. Luna RA, Nogueira DR, Varella PS, De O. Rodrigues Neto E, Norton MJR, et al. (2013) A prospective, randomized comparison of pain, inflammatory response, and short-term outcomes between single port and laparoscopic cholecystectomy. Surgical Endoscopy and Other Interventional Techniques 27: 1254–1259.

38. Ma J, Cassera MA, Spaul GO, Hannull CW, Hansen PD, et al. (2011) Randomized Controlled Trial Comparing Single-Port Laparoscopic Cholecystectomy and Four-Port Laparoscopic Cholecystectomy. Annals of Surgery 254: 22–27.

39. Madureira FAV, Manso JEF, Madureira Fo D, Igliaes ACG (2013) Randomized clinical study for assessment of incision characteristics and pain associated with LESS versus laparoscopic cholecystectomy. Surgical Endoscopy and Other Interventional Techniques 27: 1099–1015.

40. Marks JM, Phillips MS, Tacchino R, Roberts K, Onders R, et al. (2013) Single-Incision Laparoscopic Cholecystectomy Is Associated with Improved Cosmesis Scoring at the Cost of Significantly Higher Hernia Rates: 1-Year Results of a Prospective Randomized, Multicenter, Single-Blinded Trial of Traditional Multiport Laparoscopic Cholecystectomy vs Single-Incision Laparoscopic Cholecystectomy. Journal of the American College of Surgeons 216: 1037–1048.

41. Mehmedo Z, Subhan A, Ali N, Rasul S, Iqbal M, et al. (2010) Four port versus single incision laparoscopic cholecystectomy. Journal of Surgery Pakistan (International) 15: 122.

42. Novitsky YW, Kercher KW, Czerniack DR, Kaban GK, Kherra S, et al. (2005) Advantages of mini-laparoscopic vs conventional laparoscopic cholecystectomy: results of a prospective randomized trial. Archives of surgery (Chicago, Ill : 1960). pp. 1178–1180.

43. Oifie DJ, Jiang O, Iqbal CW, Sharp SW, Snyder CL, et al. (2013) Single incision versus standard 4-port laparoscopic cholecystectomy: A prospective randomized trial. Journal of Pediatric Surgery 48: 209–214.

44. Pan MX, Jiang ZS, Cheng Y, Xu XP, Zhang Z, et al. (2013) Single-incision vs three-port laparoscopic cholecystectomy: Prospective randomized study. World Journal of Gastroenterology 19: 394–398.

45. Poon CM, Chan KW, Lee DWH, Chan KC, Ko CW, et al. (2003) Two-port vs four-port laparoscopic cholecystectomy: A prospective randomized controlled trial. Surgical Endoscopy and Other Interventional Techniques 17: 1624–1627.

46. Rasic Z, Schwarz D, Nesev VA, Zoricic I, Sever M, et al. (2010) Single incision laparoscopic cholecystectomy—a new advantage of gallbladder surgery. Coll Antropol 34: 595–598.

47. Saad S, Skarret L, Sauerland S (2013) Randomized clinical trial of single-port, minilaparoscopic and conventional laparoscopic cholecystectomy. British Journal of Surgery 100: 339–349.

48. Sarli L, Isaco D, Gobbi S, Porinini C, Ferro M, et al. (2003) Randomized clinical trial of laparoscopic cholecystectomy performed with mini-instruments. British Journal of Surgery 90: 1343–1346.

49. Sasaki A, Ogawa M, Tono C, Obara S, Hossi N, et al. (2012) Single-port Versus Multiport Laparoscopic Cholecystectomy: A Prospective Randomized Clinical Trial. Surgical Laparoscopic Endoscopy & Percutaneous Techniques 22: 396–399.

50. Schmidt J, Sparenberg C, Fraunhofer S, Zirngibl H (2002) Sympathetic nervous system activity during laparoscopic and needlescopic cholecystectomy: A prospective randomized study. Surgical Endoscopy, pp. 476–480.

51. Schwenk W, Neusicker J, Mall J, Bolan M, Miller JM (2000) Prospective randomized blinded trial of pulmonary function, pain, and cosmetic results after laparoscopic vs. microlaparoscopic cholecystectomy. Surgical Endoscopy, pp. 345–348.

52. Sinan D, Demirbas S, Ozor MT, Saculli L, Akyol M (2012) Single-incision Laparoscopic Cholecystectomy Versus Laparoscopic Cholecystectomy: A Prospective Randomized Study. Surgical Laparoscopic Endoscopy & Percutaneous Techniques 22: 12–16.

53. Tsiroussiamis EC, Tsioussiamis KE, Pappas-Gogos G, Fanaros C, Brantatos N, et al. (2010) Different pain scores in single transumbilical incision laparoscopic cholecystectomy versus classic laparoscopic cholecystectomy: a randomized controlled trial. Surgical Endoscopy and Other Interventional Techniques 24: 1042–1046.

54. Tilmaz H, Arun O, Apilogullari S, Acar F, Alptekin H, et al. (2013) Effect of laparoscopic cholecystectomy techniques on postoperative pain: a prospective randomized study. Journal of the Korean Surgical Society 83: 149–153.

55. Tzipi M, Yetsaouk A, Leung D, Salhab R, Denham W, et al. (2013) Single-incision results in similar pain and quality of life scores compared with multi-incision laparoscopic cholecystectomy: A blinded prospective randomized trial of 100 patients. Surgery 154: 662–670.

56. Zheng MW, Qin MF, Zhao HZ (2012) Laparoendoscopic single-site cholecystectomy: A randomized controlled study. Minimally Invasive Therapy & Allied Technologies 21: 113–117.

57. Ainslie WG, Catton JA, Davides D, Dexter S, Gibson J, et al. (2003) Micropuncture cholecystectomy vs conventional laparoscopic cholecystectomy: a randomized controlled trial. Surgical Endoscopy, pp. 766–772.

58. Khorgami Z, Shoo S, Anbava T, Soroush A, Nasir S, et al. (2013) A Randomized Clinical Trial Comparing 4-Port, 3-Port, and Single-Incision Laparoscopic Cholecystectomy. J Invest Surg.

59. Zehetner J, Pelipad D, Dardzierski A, Mason RJ, Lipham JC, et al. (2013) Single-access laparoscopic cholecystectomy versus classic laparoscopic cholecystectomy: A systematic review and meta-analysis of randomized controlled trials. Surgical Laparoscopy, Endoscopy and Percutaneous Techniques 23: 233–243.

60. Herreeman D, da Costa DW, Vrouwenraets BC, van Wagenen BD, Lagarde SM (2013) Laparoscopic partial cholecystectomy for the difficult gallbladder: a systematic review. Surgical Endoscopy and Other Interventional Techniques 27: 351–356.

61. Gurusamy KS, Vaughan J, Ramamoorthy R, Fusi G, Davidson BR (2013) Minipoints versus standard ports for laparoscopic cholecystectomy. Cochrane Database of Systematic Reviews.

62. Grégoire L, San C, Bai J (2013) Single Incision Versus Conventional Laparoscopic Cholecystectomy Outcomes: A Meta-Analysis of Randomized Controlled Trials. PloS One 8.

63. Vilailonga R, Barbaros U, Sumer A, Demirtel T, Fort JM, et al. (2012) Single-port transumbilical laparoscopic cholecystectomy: A prospective, randomized comparison of clinical results of 140 cases. Journal of Minimal Access Surgery 8: 397–399.

64. Aabakken L, Hayashi M, Kamata K, Shimizu T, Hirokawa F, et al. (2011) Impact of single-port cholecystectomy on postoperative pain. British Journal of Surgery 98: 991–995.

65. Elwan AM, Abomera MA, Arwa NS, Al Makarem MA (2013) Comparative study between two-port and four-port laparoscopic cholecystectomy.

66. Houglun DC, Hawkins N, Janzen JP, Scott DA, Izler R, et al. (2011) Conducting indirect-treatment-comparison and network-meta-analysis studies: report of the ISPOR Task Force on Indirect Treatment Comparisons Good Research Practices: part 2. Value Health 14: 429–437.

Different Kinds of Laparoscopic Cholecystectomy