Single Incision versus Conventional Laparoscopic Cholecystectomy Outcomes: A Meta-Analysis of Randomized Controlled Trials

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Abstract

Background: Previous meta-analyses that compared the outcome of SILC and CLC have not presented consistent conclusions. This meta-analysis was performed after adding many recent RCTs, to clarify this issue.

Methods: Relevant articles published in English were identified by searching PubMed, Embase, Web of Knowledge, and the Cochrane Controlled Trial Register from January 1997 to February 2013. Reference lists of the retrieved articles were reviewed to identify additional articles. Primary outcomes (postoperative pain scores, cosmetic score, and length of incision) and secondary outcomes (operating time, blood loss, conversion rates, postoperative complications, postoperative hospital stay, time to initial oral intake, and time to resume work) were pooled. Quantitative variables were calculated using the weighted mean difference (WMD), and qualitative variables were pooled using odds ratios (OR).

Results: 25 appropriate RCTs were identified from 2128 published articles. 1841 patients were treated, 944 with SILC and 897 with CLC. SILC was superior to CLC in cosmetic score (WMD = 1.155, $P<0.001$), shorter length of incision (WMD = -3.285, $P = 0.029$), and postoperative pain within 12 h (VAS in 3-4 h, WMD = -0.704, $P = 0.026$; VAS in 6-8 h, WMD = -0.613, $P = 0.010$). CLC was superior to SILC in operating time (OT) (WMD = 13.613, $P<0.001$) and need of additional instruments (OR = 7.448, $P<0.001$). Other secondary outcomes were similar.

Conclusions: SILC offered a better cosmetic result and less postoperative pain for patients with uncomplicated cholelithiasis or polypoid lesions of the gallbladder. However, SILC was associated with a longer OT and required additional instruments.

Introduction

Since the first laparoscopic cholecystectomy (LC) was performed by Mühe et al [1] in 1985, conventional laparoscopic cholecystectomy (CLC) has become the gold standard for treatment of benign gallbladder disease. The concept of minimally invasive surgery has expanded to include smaller wounds and improved cosmesis. Navarra et al [2] first reported transumbilical single-incision laparoscopic cholecystectomy (SILC) in 1997, and proposed that SILC might be associated with less pain and reduced hospitalization. Subsequent comparative studies have reported that SILC was a safe and feasible procedure with better cosmetic results and less postoperative pain [3-5]. There were some drawbacks, however. SILC did not seem to offer any cosmetic advantage over CLC [6], had greater postoperative pain at 4 hours, and was associated with a longer operating time (OT) [7].

Nine meta-analyses [8-16] based on randomized controlled trials (RCTs) have been performed to compare SILC and CLC related outcomes. These studies confirmed the safety and feasibility of SILC. Other findings have not been consistent. Eight meta-analyses showed that SILC offered a better cosmetic score than CLC, while Sajid et al [12] reported no difference between the two. Hao and Arezzo et al [9,16] found that SILC patients have less postoperative pain during the first 24 h, in contrast to the other eight meta-analyses. Two meta-analyses [12,15] noted additional ports had to be inserted with CLC and a higher procedure failure rate with SILC. The other seven meta-analyses did not have these findings. In addition, the number of the RCTs (range: 5-15) included in these meta-analyses was much smaller than more recent RCTs.

These contradictions make it necessary to more closely compare SILC and CLC; in particular, to evaluate whether SILC is associated with less postoperative pain and better cosmetic results and whether SILC is associated with a higher procedure failure rate and longer OTs. This comprehensive meta-analysis included many recent RCTs and was systematically conducted to verify advantages and limits of these two procedures.

Materials and Methods

A meta-analysis protocol was drafted before the initial search was started. The meta-analysis was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement issued in 2009 [17].

Literature Search

We searched PubMed, Web of Knowledge, Embase and the Cochrane Controlled Trial Register to identify relevant articles published from January 1, 1997 to February 26, 2013 using the search phrases ("single port" OR "single incision" OR "single site" OR "LESS") AND (laparoscopy OR laparoscopic) AND cholecystectomy. Appropriate adjustments were required according to the database. Filters were used in PubMed, Embase and Web of Knowledge to exclude animal and non-English studies. A manual search of published meta-analyses and relevant articles was performed to identify additional articles.

Article Selection

The process of article selection was based on the PRISMA [17] flow diagram. Selected studies met the following criteria: (a) RCT design; (b) compared SILC and CLC; (c) revealed at least one of the primary or secondary outcomes mentioned below; and (d) were published in English. Articles were excluded if: (a) the surgery was not cholecystectomy; (b) single incision was not mentioned; (c) it was a retrospective study, prospective nonrandomized study, animal study, review, letter, meeting, or comment. When multiple published articles from the same study were available, the report with the most detailed information was selected.

Data Extraction

Primary outcomes evaluated included postoperative pain score, cosmetic score, and length of incision. Pain scores from RCTs using a visual analogue scale/score (VAS) were pooled to assess postoperative abdominal pain. Four postoperative time points were used to evaluate pain, 3 to 4 h, 6 to 8 h, 12 h, and 24 h. Cosmetic score was rated using a 10-point scale (0-worst to 10-best).

Secondary measures evaluated included intraoperative outcomes (OT, blood loss, conversion rates), postoperative complications (wound complications, incisional hernia, bile leakage, retained stones, bile duct injury and bleeding), and recovery outcomes (length of postoperative hospital stay, time to initial oral intake, and time to resume work). Conversion rates included operations that were converted to open or that required additional instruments. Additional added instruments were defined as situations where it was necessary to use more trocars than planned or where they were needed to enhance the exposure of Calot's triangle for gallbladder retraction.

Patient characteristics (number of patients, gender, age, body mass index, American Society of Anesthesiology rating, presence of acute cholecystitis, history of prior gastrointestinal surgery, surgical technique, and follow-up time) were also recorded. If the above data was not available in the published study, the authors were contacted and asked to supply the information.

Assessment of Study Quality

The literature search, article selection, data extraction and assessment of study quality were completed independently by two authors (Geng and Sun). Discrepancies were resolved by discussion. When a consensus could not be reached, a third author (Bai) broke the tie. The Jadad's revised rating scale [18] of each RCT is shown in Table 1. RCT randomization that was performed using a computer generated number and concealed in an opaque and sealed envelope (or similar method) was considered appropriate. Use of a non-transparent dressing covering the abdomen (or similar method) during the entire hospitalization was considered to be appropriate double blinding. A scale from 4 to 7 was considered a high-quality RCT.

Statistical Analysis

Continuous variables (OT, blood loss, postoperative hospital stay, time to initial oral intake, time to resume work, postoperative pain score, cosmetic score, and length of incision) were combined using the weighted mean difference (WMD). The method of Hozo et al [19] was used if variables were provided as medians or/and ranges instead of a mean with a standard deviation. Binary variables (conversion rate, postoperative complications) were pooled using an odds ratio (OR).

Homogeneous data was evaluated using fixed effect models. The inverted variance method was used for continuous variables and the Mantel-Haenszel method for binary variables. Random effect models based on the DerSimonian & Laird method were used to calculate the combined outcomes of both continuous and binary variables when heterogeneity existed. $P<0.05$ was considered statistically significant.

Heterogeneity was identified using a chi-square-based Q-test ($P \leq 0.10$) and I^2 index (I^2 exceeding 50 percent). If heterogeneity was found, a meta-regression based on the Restricted Maximum Likelihood (REML) method was conducted to identify any related factors ($P<0.05$ was considered significant). Subgroup analyses were conducted to identify potential sources of heterogeneity when the meta-regression was not adequate (less than 10 studies reported the outcome) or as a supplementary method.

Sensitivity analyses were performed to examine the effect of excluding lower quality studies. Publication bias was evaluated using Egger's regression test, with $P<0.05$ indicating statistically significant publication bias. The confidence interval

Table 1. Jadad's revised rating scales of the 25 studies included in the meta-analysis.

| Study | Country | Randomization | | Double Blinding | Withdraws and Dropouts | Jadad's Score[a] |
		Generate	Hide			
Saad [22], 2013	Germany	2	2	2	1	7
Madureira [23], 2013	Brazil	1	0	0	1	2
Chang [24], 2013	Singapore	1	0	1	1	3
Ostlie [25], 2013	USA	2	0	0	0	2
Pan [26], 2013	China	2	2	0	1	5
Sinan [27], 2012	Turkey	2	1	0	0	3
Vilallonga [28], 2012	Spain	1	0	0	0	1
Phillips [29], 2012	USA	1	0	2	1	4
Noguera [30], 2012	Spain	1	0	0	0	1
Sasaki [31], 2012	Japan	2	0	0	1	3
Luna [32], 2012	Brazil	1	0	0	0	1
Leung [33], 2012	USA	1	0	2	0	3
Zheng [34], 2012	China	2	2	0	0	4
Marks [35], 2011	USA	1	1	1	0	3
Ma [36], 2011	Portland	2	1	0	0	3
Lirici [37], 2011	Italy	2	2	2	0	6
Lai [38], 2011	China	2	2	0	1	5
Cao [39], 2011	China	1	2	0	0	3
Bucher [40], 2011	Switzerland	2	1	0	1	4
Aprea [41], 2011	Italy	1	2	0	0	3
Tsimoyiannis [42], 2010	Greece	1	2	1	0	4
Lee [43], 2010	China	1	2	0	1	4
Mehamood [44], 2010	Pakistan	1	2	0	0	3
Rasic [45], 2010	Croatia	2	0	0	0	2
Bresadola [46], 1999	Italy	1	0	0	0	1

[a] 4 to 7 as high-quality, otherwise, considered low-quality.

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(CI) was established at 95%. Statistical analyses were carried out using Stata11.0 software (Stata Corporation, USA).

Results

Identification of Studies and Quality of the RCTs

27 RCTs [20-46] were extracted from 2128 publications identified from databases and other sources. Requested data could not be obtained from the author in two ongoing trials [20,21]. The PRISMA [17] flow diagram for this meta-analysis is presented in Figure 1. Many studies were called randomized without defining the method of randomization or blinding and whether patients withdrew or dropped out (Table 1). Only nine high-quality (Jadad's revised rating scale, 4 to 7) articles were included in the meta-analysis (Table 1).

Characteristics of Included RCTs

1841 patients (944 with SILC, 897 with CLC) were identified to be included in the meta-analysis. Table S1 shows the general characteristics, including sample size, M/F ratio, age, body mass index (BMI), and American Society of Anesthesiology (ASA) score. Patients with a history of gastrointestinal surgery were reported by Ma (67% in SILC, and 76% in CLC) and Bucher (39% in SILC, and 36% in CLC) et al [36,40]. Only Vilallonga, Leung and Bucher et al [28,33,40] reported SILC in patients with acute cholecystitis. CLC was performed using 3 or 4 ports. Four techniques were used to perform SILC. Follow-up in the RCTs was usually short. General characteristics, operative techniques and follow-up time of the 25 studies are listed in Tables S1 and S2.

Quantitative Synthesis

Primary Outcomes. The postoperative pain scores were assessed in twenty one studies (Table S3). Table 2 summarizes the pooled results of the VASs. VASs from postoperative 3 to 4 h and 6 to 8h were significantly lower after SILC (P = 0.026 and 0.010, respectively). There were no significant differences in VASs at 12 h and 24h (P = 0.168 and 0.076, respectively). Thirteen studies reported cosmetic score. Three were excluded as they did not provide a ten-point scale (Table S4). The best cosmetic result was obtained with SILC (P<0.001) (Table 2). Five studies reported the length of the incision, and SILC was compared with three-port LC in one article (Table S4). The length of incision for SILC was significantly shorter than that with CLC (P = 0.029) (Table 2). Forest plots of primary outcomes are listed in Figure 2.

Secondary Outcomes. 25 studies reported OT. Five studies were excluded because there was no standard deviation (Table S5). OT with SILC was significantly longer than that with CLC (P<0.001). There was no difference in blood loss in 9 reporting articles (P = 0.352). Pooled results of OT and blood loss are listed in Table 2. The incidence of additional instruments used for SILC and CLC was 6.1% and 0.2%, respectively (Table S5). It was statistically higher for SILC than that with CLC (P<0.001) (Table 2). Among the three patients converted to open surgery, one occurred with SILC and two occurred with CLC (Table S5). The conversion to open rates of
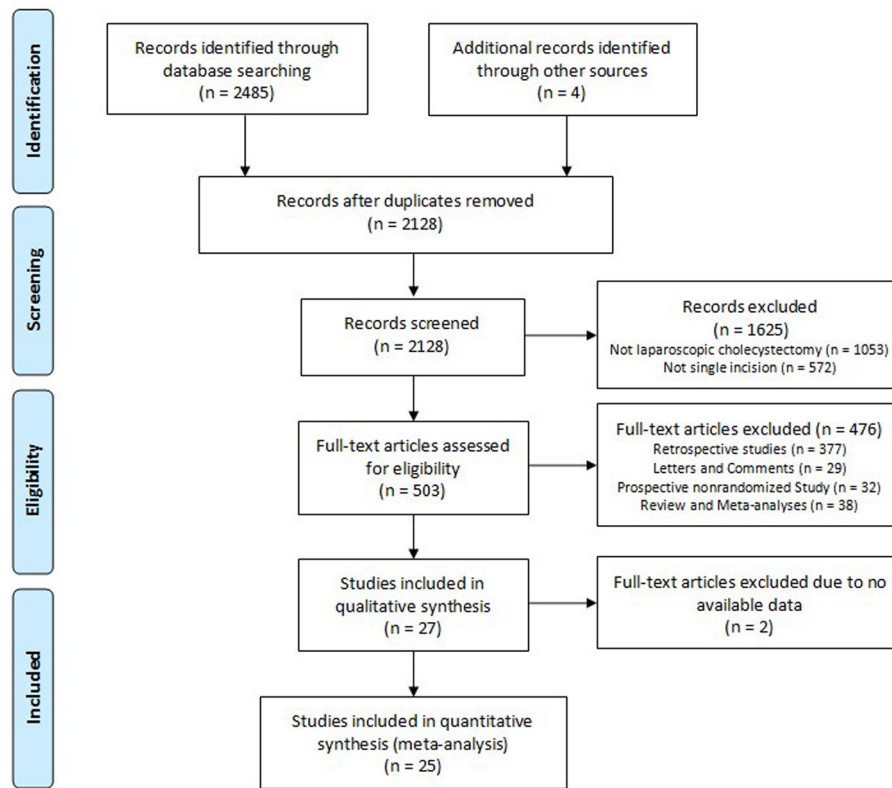
Figure 1. PRISMA flow diagram of the systematic article selection process.

SILC and CLC were 0.1% and 0.2%, respectively. There was no significant difference in the conversion to open rate ($P = 0.655$) (Table 2). Forest graphs for intraoperative outcomes are shown in Figure 3.

Only three articles included in the meta-analysis showed no complication (Table S6). The overall morbidity was 12.39% (117) for SILC and 9.48% (85) for CLC ($P = 0.220$) (Table 2). There were also no differences in the wound complications, incisional hernia, bile leakage, retained stones, bile duct injury and bleeding sub-groups ($P>0.05$) (Table 2). There were no deaths in any of the included RCTs. Forest graphs for postoperative complications are shown in Figure 4.

Pooled results of recovery outcomes are listed in Table 2. There was no significant difference in the postoperative hospital stay, time to initial oral intake, and time to resume work of patients undergoing SILC and CLC in 17 articles ($P>0.05$). The raw data of recovery outcomes are listed in Table S7. Forest graphs for recovery outcomes are shown in Figure 5.

Test of Heterogeneity

The results of heterogeneity testing are summarized in Table 2. Significant heterogeneity existed in all primary outcomes (postoperative pain scores, cosmetic score and length of incision) and some secondary outcomes (OT, blood loss, postoperative hospital stay and time to resume work).

We evaluated study quality and general and secondary characteristics of the included studies (Table 1, S1 and S2) as potential sources of methodological and clinical heterogeneity. Meta-regressions were performed for postoperative pain scores, OT and hospital stay to assess the potential reasons. Subgroup analyses were conducted by stratifying study quality (high-quality vs. low-quality, Table 1), acute cholecystitis (SILC patients with vs. without), operative technique and follow-up time (short vs. slight long period) (Table S2) to verify the accuracy of the meta-regression and assess the possible sources of heterogeneity in cosmetic score, length of incision, blood loss and time to resume work. There were no significance sources of methodological and clinical heterogeneity identified by the meta-regression and subgroup analyses (Data not shown).

Sensitivity Analysis and Publication Bias

Sensitivity analysis was conducted to assess the effect of study quality. Only length of incision results were affected by (low) quality of study (Data not shown). After low-quality studies were excluded, there was no statistically difference in length of incision ($P = 0.841$). Statistical publication bias was found in VAS in 24h, cosmetic score, OT, retained stones, and time to initial oral intake, according to Egger's test ($P<0.05$) (Table 2).

Table 2. Meta-analysis of the primary and secondary outcomes in 25 RCTs.

Outcomes	Quantitative Synthesis				Heterogeneity		Bias
	WMD/OR95% CI		z	P	I^2	P	P
Primary Outcomes							
Postoperative Pain Score[a]							
VAS in 3 to 4h	-0.704	-1.323, -0.085	2.23	0.026	56.1%	0.059	0.184
VAS in 6 to 8h	-0.613	-1.077, -0.149	2.59	0.010	74.5%	< 0.001	0.174
VAS in 12h	-0.580	-1.404, 0.244	1.38	0.168	77.8%	0.004	0.763
VAS in 24h	-0.457	-0.963, 0.048	1.77	0.076	93.8%	< 0.001	0.007
Cosmetic Score[a]	1.155	0.607, 1.703	4.13	< 0.001	92.0%	< 0.001	0.001
Length of Incision[a]	-3.285	-6.232, -0.338	2.18	0.029	96.6%	< 0.001	0.451
Secondary Outcomes							
Intraoperative Outcomes							
Operating Time[a]	13.613	9.047, 18.179	5.84	< 0.001	90.1%	< 0.001	0.005
Blood Loss[a]	1.506	-1.666, 4.679	0.93	0.352	72.0%	0.001	0.889
Additional Instrument Added	7.448	3.821, 14.518	5.90	< 0.001	0	0.867	0.931
Conversion to Open	0.686	0.132, 3.576	0.45	0.655	0	0.575	0.724
Postoperative Complications							
Wound Complications	1.336	0.842, 2.119	1.23	0.219	0	0.556	0.393
Incisional Hernia	1.937	0.658, 5.706	1.20	0.230	0	0.907	0.422
Bile Leakage	1.329	0.451, 3.912	0.52	0.606	0	0.631	0.878
Retained Stones	2.149	0.554, 8.329	1.11	0.269	0	0.933	< 0.001
Bile Duct Injury	1.000	0.165, 6.066	0.70	1.000	0	0.364	-
Bleeding	0.586	0.074, 4.639	0.51	0.613	0	0.602	-
Overall Morbidity	1.220	0.888, 1.676	1.23	0.220	0	0.903	0.689
Recovery Outcomes							
Postoperative Hospital Stay[a]	-0.127	-0.384, 0.129	0.74	0.331	91.8%	< 0.001	0.680
Initial Oral Intake	-0.196	-1.204, 0.813	0.38	0.704	0	0.775	0.012

Table 2 (continued).

Outcomes	Quantitative Synthesis				Heterogeneity		Bias
	WMD/OR95% CI		z	P	I^2	P	P
Time to Resume Work[a]	-0.527	-2.122, -1.068	0.65	0.517	94.5%	< 0.001	0.734

Continuous variables were combined by weighted mean difference (WMD); binary variables were pooled by odds ratios (OR). a: Random effect model was used; otherwise, fixed-effects model was used.

Discussion

A better cosmetic score, length of incision, and less postoperative pain within 12 h were found with SILC. CLC was associated with a shorter OT and required fewer additional instruments. There was no significant difference between SILC and CLC in regard to blood loss, open conversion rate, postoperative complications, time of hospital stay, time to initial oral intake, and time to resume work.

There were several limitations to this study. The meta-regression and subgroup analyses we performed did not account for all the sources of heterogeneity, which existed in the great majority of continuous variables (Table 2). Random effects models were used when heterogeneity existed, although the stability of the pooled analyses could not be affirmed. There was also publication bias in some of the outcomes. One potential reason is that there were many non-double-blind studies with only a small number of cases enrolled. No withdrawals or dropouts were reported in the majority of articles, and Jadad's revised rating scale for the RCTs was low (Table 1). In addition, complicated cases such as acute cholecystitis were excluded from most of studies except that of Vilallonga, Leung and Bucher et al [28,33,40]. We attempted to avoid sampling bias by requesting missing data from all the RCTs. We were not able to obtain this data from two reports [20,21]. Finally, we performed an electronic search and a manual search in order to identify any potentially relevant articles. We may have missed some meaningful articles, especially those not in English.

A major focus of this study was to determine which surgical method was associated with the least postoperative pain and best cosmetic results. In contrast to previous meta-analyses, we found a significant difference in the VAS scores at postoperative 3 to 4h and 6 to 8h. Patients undergoing SILC may have had less pain due to absence of the subcostal and xiphoid incision. The postoperative VASs could be influenced by bile leakage, intraperitoneal pressure, use of local anesthetics, peritoneal irrigation, psychological factors and type of incision [38,47-49]. These factors could also contribute to heterogeneity. Although all of RCTs reported a postoperative pain score, different time points and methods were used (Table S3). The presence of heterogeneity and publication bias prevented identification of a superior surgical technique. Future prospective double-blind randomized controlled studies will need to address the issue of postoperative pain at different time points.
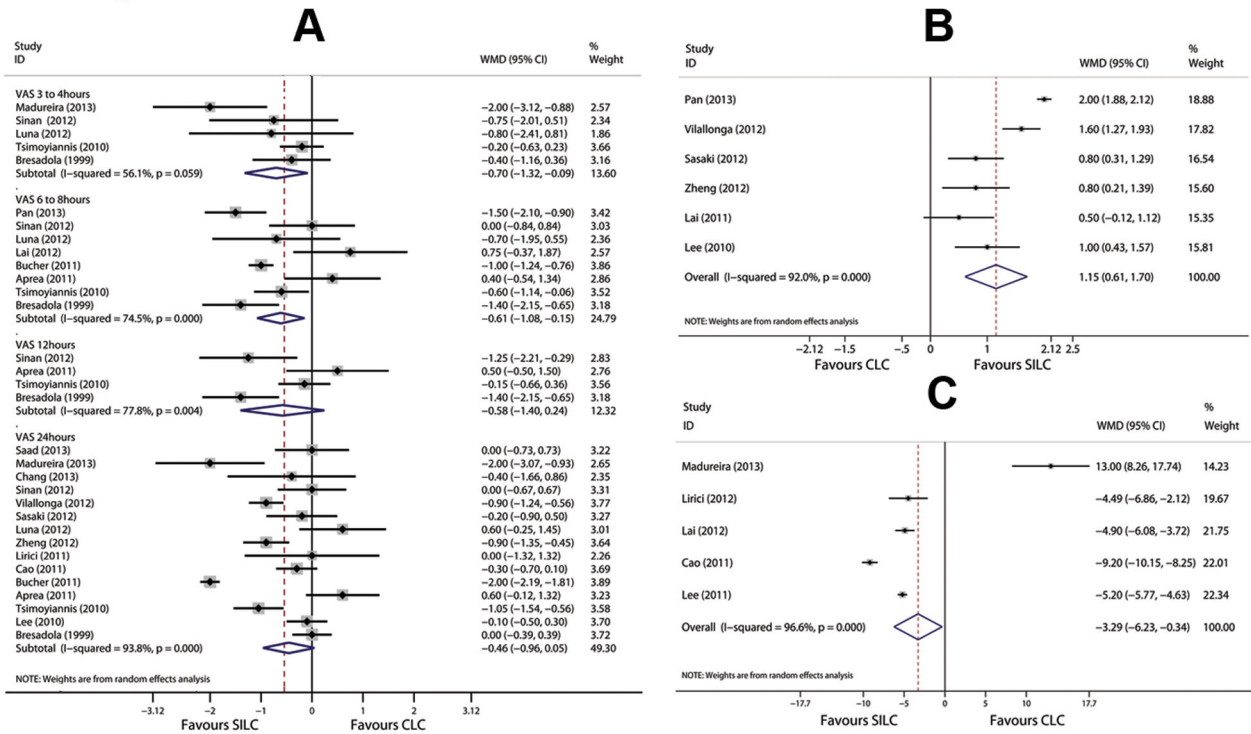
Primary Outcomes

Figure 2. Forest plots for primary outcomes included postoperative pain scores from four time points(A) cosmetic score (B) and length of incision (C). CI: confidence interval; WMD: weighted mean difference. Random effects models based on the DerSimonian & Laird methods were used as heterogeneity existed in all primary outcomes.

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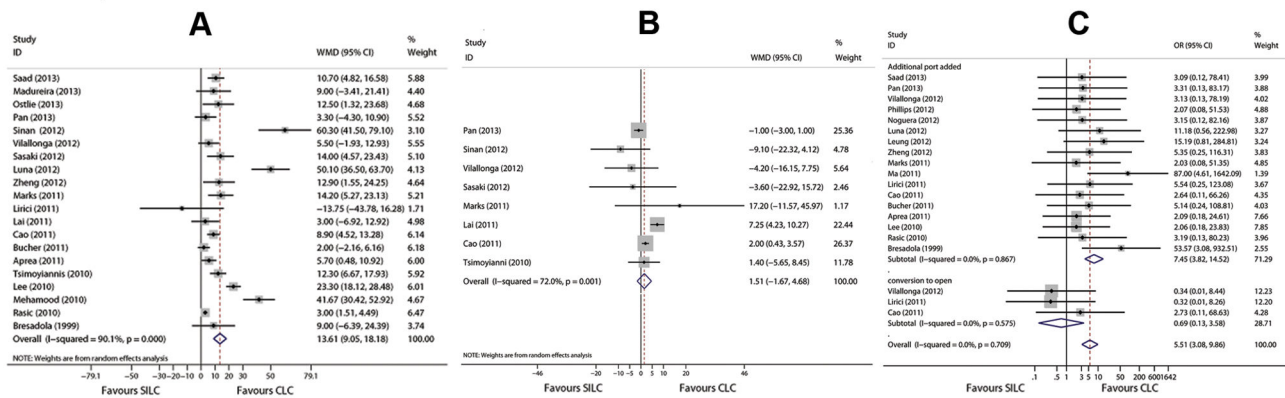
Intraoperative Outcomes

Figure 3. Forest plots for intraoperative outcomes included operating time. (A) **blood loss (B) conversion rate (C).** CI: confidence interval; WMD: weighted mean difference; OR: odds ratio. A fixed effect model was used as no statistical heterogeneity across conversion rate (C) was observed. Random effects models were used as heterogeneity existed in operating time (A) and blood loss (B).

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Most reports documented an improved cosmetic result after SILC [40,43,50]. SILC produced a shorter incision with a smaller scar. An important reason for the use of SILC was that scarless surgery is a high priority. Our study demonstrated that
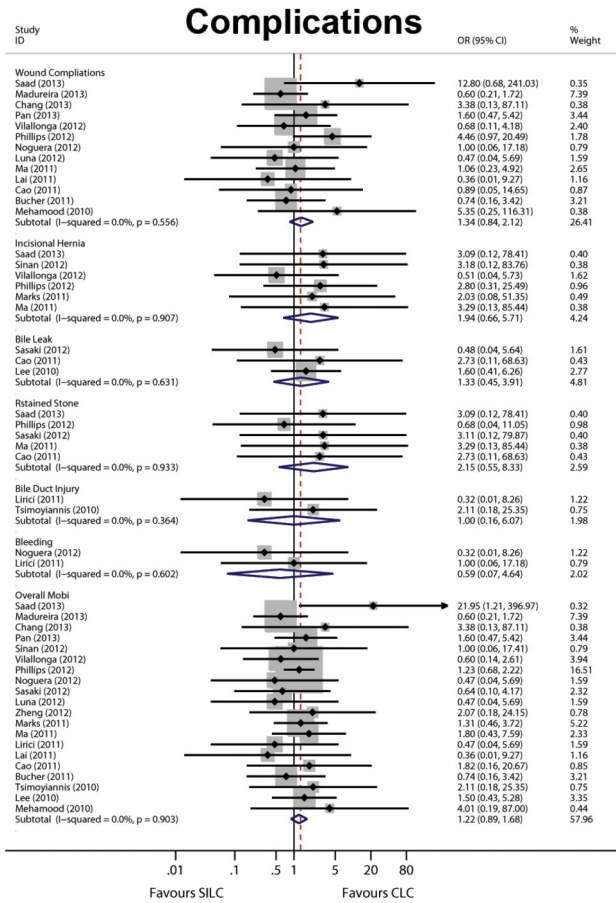
Figure 4. Forest plots for postoperative complications included wound complications, incisional hernia, bile leak, retained stones, bile duct injury and bleeding. CI: confidence interval; OR: odds ratio. A fixed effects model was used as no statistical heterogeneity across complications were observed.

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SILC was associated with a better cosmetic score and a shorter incision than CLC. Our findings regarding cosmetic score were identical to seven previous meta-analyses. The better cosmetic results with SILC may be explained by the use of a single concealed umbilical incision of short length. It was difficult to evaluate cosmetic score because of the subjective factors and environmental impact [36]. The scar may change over time, thus resulting in different outcomes. Also, the evaluation of cosmetic results currently only evaluates the postoperative abdominal incision. We found an unstable result regarding length of incision after low-quality RCTs were excluded. Large high-quality RCTs are needed to assess cosmetic results.

SILC was associated with a significantly longer OT than CLC, similar to all the other meta-analyses except that of Zhong et al [14]. It has been observed that the OT of SILC decreased significantly after the initial 10 cases, as experience is gained. No significance difference in the OT of SILC and

CLC was reported after the first 10 cases [5,46]. Only the surgeons performing the operations in one RCT included in our meta-analysis were beyond the SILC learning curve phase with proficient experience [40]. This could be partly responsible for a long OT in the SILC group and may explain the heterogeneity and publication bias. In addition, Cao et al [39] found that SILC patients with a high BMI (>24), acute cholecystitis, or a history of abdominal surgery with related abdominal adhesions exhibited longer OTs than similar CLC patients. Zahid et al [51] also reported that the inflammation and adhesions of the gallbladder, and BMI were important factors affecting OT. These types of patients were rarely included in RCTs and could explain the publication bias. A large RCT including complicated cases need to be performed. Surgeons in the study should be experienced and beyond their learning curve.

We found SILC was associated with an increased requirement for additional port insertion or instruments, similar to the meta-analysis by Sajid et al [12]. Ma et al [36] reported that 78.6 percent (11/14) additional instruments added cases in SILC were present in their learning curve phase. Little experience in SILC initial attempt could be responsible for the need to put additional ports or instruments. Furthermore, SILC could be converted to CLC in patients with acute cholecystitis, dense adhesions, Mrizzi syndrome and obesity, where there were technical problems and difficulties identifying anatomic landmarks [32,34,39,40,46].

SILC and CLC had a similar rate of postoperative complications. Wound infections were a major concern after SILC. The umbilical port could be seeded during removal of the gallbladder or with inadequate port site inspection or closure [29,52]. While SILC may be more prone to incisional hernias than CLC, because of the longer incision, we found no difference in the two methods. Follow-up was short, however, and may underestimate the final results. Hall et al [52] reported that transperitoneal sutures might increase the risk of intraoperative bile leakage. This meta-analysis found no difference in bile leakage in the two methods. Only Bresadola and Aprea et al [41,46] performed intraoperative cholangiography, which could lead to a publication bias, as it may reduce the rate of retained stones. The rate of bile duct injury was similar in both groups. This was expected as most patients were not technically complicated.

While there have been some reports of a benefit in hospital stay with SILC [40,43,50], we found no such benefit. This finding was supported by the majority of previous meta-analyses. There was no significant difference in time to resume work and time to initial oral intake. We believe that the small incision used for SILC was not significantly different from that in CLC, and did not affect recovery. Many other factors affected measurement of recovery including hospital factors, social habits, and medical insurance and so on [53]. These factors could contribute to heterogeneity and publication bias.

Conclusions

SILC was the preferred procedure for the treatment of uncomplicated gallbladder stones and polyps, as it was associated with a better cosmetic result and less postoperative
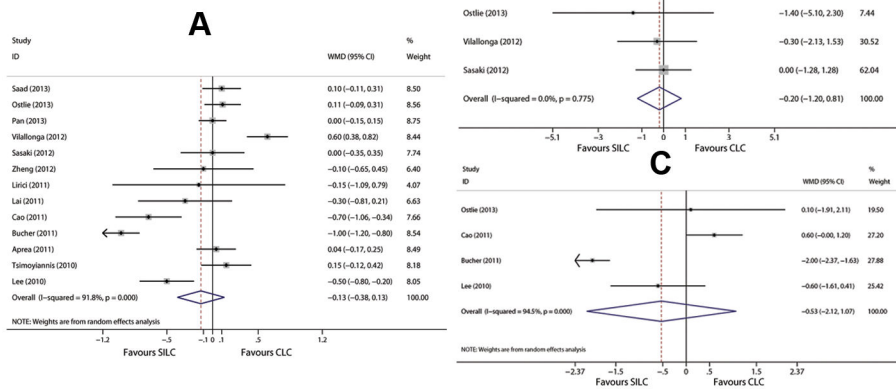
Figure 5. Forest plots for recovery outcomes included length of postoperative hospital stay (A), time to initial oral intake (B) and time to resume work (C). CI: confidence interval; WMD: weighted mean difference. Random effects models based on the DerSimonian & Laird methods were used as heterogeneity existed in hospital stay (A) and time to resume work (C). A fixed effect model was used as no statistical heterogeneity across initial oral intake (B) was observed.
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pain. There was not enough data to support SILC as the standard of care as it was associated with longer OTs and more frequently required additional instruments. A large prospective double-blind randomized controlled trial comparing SILC and CLC is needed to identify the best procedure. The presence of a learning curve for the surgeons needs to be accounted for. The effect of complicating patient factors, including acute cholecystitis, previous abdominal surgery, and severe obesity, need to identified.

Supporting Information

Checklist S1. PRISMA 2009 Checklist.
(DOC)

Table S1. General characteristics of the 25 studies included in the meta-analysis.
(DOC)

Table S2. Operative techniques and follow-up time in the 25 studies.
(DOC)

Table S3. VASs of the 25 studies included in the meta-analysis.

(DOC)

Table S4. Cosmetic results of the 25 studies included in the meta-analysis.
(DOC)

Table S5. Intraoperative outcomes of the 25 studies included in the meta-analysis.
(DOC)

Table S6. Postoperative complications of the 25 studies included in the meta-analysis.
(DOC)

Table S7. Recovery outcomes of the 25 studies included in the meta-analysis.
(DOC)

Author Contributions

Conceived and designed the experiments: LG JB. Performed the experiments: LG CS JB. Analyzed the data: LG. Contributed reagents/materials/analysis tools: LG. Wrote the manuscript: LG CS.

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