Systematic review

Meta-analysis of single-port *versus* conventional laparoscopic cholecystectomy comparing body image and cosmesis

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Background: **The purpose of this study was to evaluate improvements in cosmetic results and postoperative morbidity for single-incision laparoscopic cholecystectomy (SILC) in comparison with multiport laparoscopic cholecystectomy (MLC).**

Methods: **A literature search was undertaken for RCTs comparing SILC with MLC in adult patients with benign gallbladder disease. Primary outcomes were body image and cosmesis scores at different time points. Secondary outcomes included intraoperative and postoperative complications, postoperative pain and frequency of port-site hernia.**

Results: **Thirty-seven RCTs were included, with a total of 3051 patients. The body image score favoured SILC at all time points (short term: mean difference (MD) −2·09, $P < 0·001$; mid term: MD −1·33, $P < 0·001$), as did the cosmesis score (short term: MD 3·20, $P < 0·001$; mid term: MD 4·03, $P < 0·001$; long-term: MD 4·87, $P = 0·05$) and the wound satisfaction score (short term: MD 1·19, $P = 0·03$; mid term: MD 1·38, $P < 0·001$; long-term: MD 1·19, $P = 0·02$). Duration of operation was longer for SILC (MD 13·56 min; $P < 0·001$) and SILC required more additional ports (odds ratio (OR) 6·78; $P < 0·001$). Postoperative pain assessed by a visual analogue scale (VAS) was lower for SILC at 12 h after operation (MD in VAS score −0·80; $P = 0·007$). The incisional hernia rate was higher after SILC (OR 2·50, $P = 0·03$). All other outcomes were similar for both groups.**

Conclusion: **SILC is associated with better outcomes in terms of cosmesis, body image and postoperative pain. The risk of incisional hernia is four times higher after SILC than after MLC.**

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Introduction

Benign gallstone disease is a common finding in developed countries, affecting 10–15 per cent of the adult population[1]. Approximately 20 per cent of those affected develop symptomatic gallstone disease requiring surgical removal of the gallbladder, making cholecystectomy one of the most common procedures in general surgery. First performed in 1985[2], laparoscopic three-port cholecystectomy rapidly established itself as the standard for the treatment of symptomatic cholelithiasis. Owing to its efficacy, safety and shorter convalescence, the technique was considered superior to open cholecystectomy even in the absence of evidence derived from randomized trials[3,4].

In an attempt to improve postoperative morbidity and cosmetic results further, new laparoscopic techniques using fewer incisions were developed, such as three-port and single-port cholecystectomy, as well as natural orifice transluminal endoscopic surgery[5–8]. Although it has increased gradually in popularity since the first publication in 1997[7], single-incision laparoscopic cholecystectomy (SILC) is still not in widespread use and its acceptance as a routine practice has remained controversial. This is partly because of the lack of high-quality evidence of improved outcome using this technique[9–11].

The main reason for performing SILC is improved cosmesis and body image. However, the extent to which this technique contributes to improved outcomes assessed by validated scores in RCTs is still unknown. There are few data in the literature regarding long-term outcome, quality of life (QoL), cost-effectiveness and complication rates assessed by means of validated classification tools. Therefore, this systematic review and meta-analysis was conducted to compare the single-port and conventional multiport laparoscopic cholecystectomy (MLC) techniques in terms of cosmesis and body image, short- as well as long-term postoperative outcomes, and QoL in patients undergoing laparoscopic cholecystectomy for benign gallbladder disease.

Methods

A systematic review protocol was registered and made available online in the international PROSPERO database (CRD42015019347). This study was reported in compliance with the PRISMA checklist for systematic reviews and meta-analyses[12].

Eligibility criteria

Published and ongoing RCTs were included. Animal studies were excluded. Retrospective studies, quasi-randomized trials, and prospective cohort and case–control studies were excluded as there is inherent selection bias. There was no language restriction. Participants in the included studies were adults undergoing elective or emergency laparoscopic cholecystectomy for any reason (symptomatic gallstones, acute and chronic cholecystitis, including acalculous, or any other benign condition such as polyps). SILC with or without additional ports (intention-to-treat analysis) as well as MLC with two or more ports (typically 4) were included.

Primary outcomes

Patient satisfaction with cosmesis and body image at different time points after surgery was assessed by means of the validated cosmesis scale (ranging from 3 to 24, with a higher score indicating a greater degree of satisfaction with the scar) and the Body Image Questionnaire (BIQ) (ranging from 5 to 20 points, with a low score signifying better body image)[13], or using a linear wound satisfaction score ranging from 1 (worst) to 10 (best).

Secondary outcomes

Secondary outcomes included intraoperative blood loss, use of additional ports, rate of conversion to open cholecystectomy, duration of operation, postoperative pain, postoperative analgesia use, intraoperative and postoperative complications, length of hospital stay, costs, time to return to work and postoperative QoL.

Search methods for identification of studies

The bibliographic databases MEDLINE, PubMed, the Cochrane Library, Embase and Scopus were searched for relevant articles from 1 January 1995 to 30 September 2015. The search terms single incision, single port, single site, single scar, single trocar, single access, single incision multiport laparoendoscopic, transumbilical, transumbilical single-port, laparo-endoscopic single-site, minimal invasive, minimal access, single umbilical incision, umbilical port-only, SILS, SILC, LESS, TUSPS and SIMPLE, and medical subject (MeSH) headings cholecystectomy, laparoscopic cholecystectomy, surgery, laparoscopic surgery, gallbladder surgery, laparoscopic gallbladder surgery, gallbladder removal, laparoscopic gallbladder removal, gallbladder resection and laparoscopic gallbladder resection, were used in various combinations. Two authors reviewed relevant articles independently and duplicates were removed. Abstracts, letters, editorials and opinion articles were excluded. Discrepancies were resolved at an official meeting of the investigators.

Data extraction and analysis

Data collection was carried out by two independent reviewers using a predefined electronic protocol (available at www.review-net.com), including first author's name, publication year, study design, total number of patients, number of patients in the SILC and MLC groups, age (mean, median, s.d., s.e.m., range, i.q.r.), sex ratio and preoperative BMI (weight and height). Data collected on the primary outcome comprised postoperative scores for satisfaction with cosmesis and body image at different time points. The following data were collected for the secondary endpoints: type of operation, surgical technique, duration of surgery (mean, median, s.d., s.e.m., range, i.q.r.), blood loss (mean, median, s.d., s.e.m., range, i.q.r.), rate of conversion to open cholecystectomy, intraoperative and postoperative complications, type of complications, postoperative pain (measured using a visual analogue scale (VAS) ranging from 0 indicating no pain to 10 for worst imaginable pain), postoperative use of analgesics, length of postoperative hospital stay (mean, median, s.d., range, i.q.r.), postoperative QoL, costs, mortality and reason for death. Authors of the individual trials were contacted for missing information. An intention-to-treat analysis was performed whenever possible. When the mean and s.d. were not available, they were calculated from the median and range using an approved calculator.

Data synthesis and assessment of heterogeneity

Statistical meta-analysis was performed using Review Manager version 5.3 for Mac (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark), and Comprehensive Meta-Analysis version 2 (Biostat, Englewood, New Jersey, USA; http://www.comprehensive.com) was used for single-group analysis.

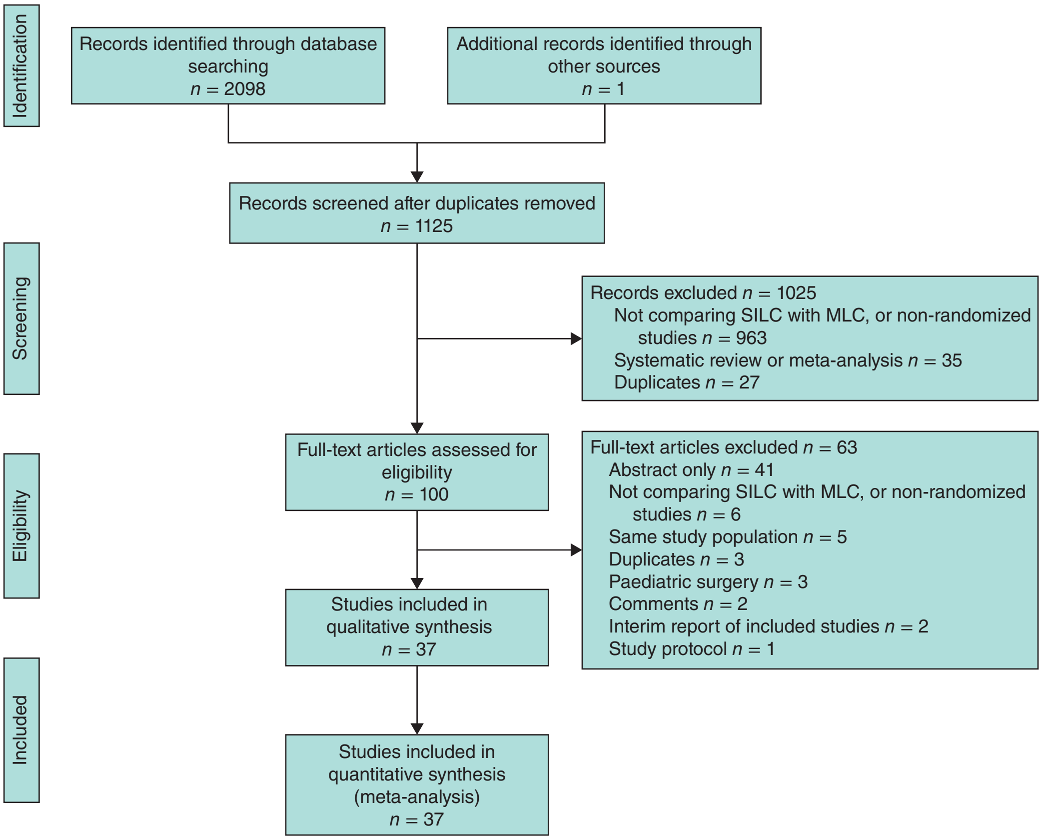

Fig. 1 Flow diagram showing selection of articles for review. SILC, single-incision laparoscopic cholecystectomy; MLC, multiport laparoscopic cholecystectomy

A quantitative synthesis was used because the included studies were sufficiently homogeneous. A narrative synthesis of the findings from the included studies was prepared. Intervention effects for each study and overall effect estimates were calculated as odds ratios (ORs) for dichotomous outcomes and weighted mean differences (MDs) for continuous outcomes, with 95 per cent confidence intervals. Two-sided P values for each outcome were calculated and $P < 0{\cdot}050$ was considered significant. The degree of heterogeneity among results was estimated by using the Cochrane Q statistic (with $P < 0{\cdot}100$ considered to indicate significant heterogeneity) and the I^2 statistic (a value exceeding 50 per cent indicated significant heterogeneity). I^2 describes the percentage of total variation across studies that is due to heterogeneity rather than chance. A random-effects model was used for meta-analysis if either of the two statistics was significant; otherwise a fixed-effect model was used. In the fixed-effect model, the only source of uncertainty is within-study error. In the random-effects model, there is this same source of uncertainty plus between-studies variance. Thus the fixed-effect model provides the best estimate of a common treatment effect, whereas the random-effects model provides an estimate of the average treatment effect[14]. The evidence of publication bias was assessed by inspection of a funnel plot.

Results

Search results

A total of 2098 records were identified through electronic searches of Embase (491), MEDLINE (550), PubMed (2), the Cochrane Library (202) and Scopus (853). In addition, the most recent unpublished RCT, which was not yet available at the time of the searches, was provided by one of the authors[15]. After excluding duplicates, 1125 records remained. These records were screened for relevance by title and abstract, and 1025 of them were excluded. The remaining 100 full-text articles were assessed for eligibility. Of these, 63 references were excluded. No additional RCTs were identified through screening of the citation lists of relevant publications. In total, 37 studies were included (*Fig. 1*).

Table 1 Baseline patient characteristics

		No. of patients		Age (years)*		Sex ratio (F : M)		BMI (kg/m²)*		Follow-up
Reference	Country	SILC	MLC	SILC	MLC	SILC	MLC	SILC	MLC	(weeks)
Abd Ellatif *et al.*[35]	Egypt	125	125	47·7(10·6)	46·9(11·4)	95 : 30	88 : 37	26·9(5·5)	29·5(5·6)	26
Aprea *et al.*[32]	Italy	25	25	45·5(9·4)	44(10)	16 : 14‡	19 : 6	25·9(5·8)	23·7(4·6)	n.r.
Borle *et al.*[50]	India	30	30	42·3(11·8)	40·2(14·4)	20 : 10	23 : 7	23(1·8)	23·4(1·8)	4
Bresadola *et al.*[26]	Italy	28	37	42(20)	45(15)	19 : 9	22 : 15	n.r.	n.r.	n.r.
Brown *et al.*[33]	USA	40	39	45·1(14·5)	43(14·8)	29 : 11	32 : 7	29·4(5·1)	30·3(6·9)	4
Bucher *et al.*[22]	Switzerland	75	75	45·8(16·4)	44(9·7)	n.r.	n.r.	27·3(3·4)	25·8(3·9)	4
Cao *et al.*[34]	China	57	51	62·2(5·1)	59·7(4·4)	34 : 23	29 : 22	28·6(4·4)	29·1(5·1)	4
Chang *et al.*[44]	Singapore	51	50	48·2(12·5)	52·5(13·1)	31 : 20	30 : 20	25·3(4·5)	25·8(6·5)	26
Deveci *et al.*[47]	Turkey	50	50	42·9(12)	40·1(12·2)	45 : 5	43 : 7	27·9(5)	28·1(5·2)	52
Herrero Fonollosa *et al.*[36]	Spain	26	24	45(12)	49(12)	20 : 6	14 : 10	26(4)	25(2)	26
Jørgensen *et al.*[21]	Denmark	60	60	45·5 (34·3–54·0)†	46 (33·0–56·0)†	60 : 0	60 : 0	26·6 (23·9–28·4)†	24 (22·8–29·1)†	52
Justo-Janeiro *et al.*[45]	Mexico	18	19	42·8(15·8)	44·1(17·5)	16 : 2	13 : 6	28·2(3·1)	27·6(4·7)	1
Khorgami *et al.*[17]	Iran	30	60	43·8(12·7)	41·6(11·1)	22 : 8	41 : 19	27·9(4·3)	27·7(4·2)	52
Lai *et al.*[48]	Hong Kong	24	27	51·7(13·3)	54·3(12)	16 : 8	16 : 11	25(3)	24·4(2·8)	12
Lee *et al.*[37]	Taiwan	35	35	51(13·5)	53·3(15·5)	22 : 13	20 : 15	24·2(3·4)	25·8(3)	26
Lirici *et al.*[38]	Italy	20	20	44·8(9·3)	47·8(10·8)	14 : 6	14 : 6	24·2(3·2)	25·4(3·5)	4
Luna *et al.*[23]	Brazil	20	20	n.r.	n.r.	n.r.	n.r.	n.r.	n.r.	4
Lurje *et al.*[15]	Switzerland	48	48	48(16)	44(1)	33 : 15	29 : 19	25(3)	26(5)	52
Ma *et al.*[24]	USA	21	22	57·3(16)	45·8(11·9)	n.r.	n.r.	28·2(5·3)	30·7(6·1)	33
Madureira *et al.*[25]	Brazil	28	29	50(9·8)	56(17)	n.r.	n.r.	28·6(7·7)	25·5(4·4)	26
Marks *et al.*[16]	USA	119	81	45·8(9·8)	44(8·7)	91 : 28	57 : 24	29·5(7·7)	31·5(6·7)	52
Mehmood *et al.*[27]	Pakistan	30	30	44·4(8·6)	42·7(9·1)	28 : 2	26 : 4	n.r.	n.r.	n.r.
Noguera *et al.*[46]	Spain	20	20	49(4)	60(5)	17 : 3	16 : 4	28(4)	30(1)	52
Pan *et al.*[39]	China	49	53	43·8(14)	45·2(1)	26 : 23	31 : 22	24·3(6)	25·1(5)	8
Rašić *et al.*[40]	Croatia	48	50	44(6)	44(5·7)	26 : 22	32 : 18	27(4)	27(4)	4
Rizwi *et al.*[28]	Pakistan	100	100	40·8(7·9)	42·5(8·7)	59 : 41	57 : 43	n.r.	n.r.	n.r.
Saad *et al.*[19]	Germany	35	35	45(17)	49(14)	7 : 28	9 : 26	25·4(2·5)	25·4(3·1)	52
Sasaki *et al.*[20]	Japan	27	27	56·6(14·2)	58·2(12·3)	13 : 14	13 : 14	24·4(3)	24·9(3·4)	4
Sinan *et al.*[41]	Turkey	17	17	48·5(8·9)	48·7(14·3)	13 : 4	9 : 8	27·3(3·1)	27·2(2·9)	39
Solomon *et al.*[18]	USA	22	11	38·4(3·3)	35·5(4·1)	22 : 0	11 : 0	31·8(1·4)	31·4(2·2)	4
Telciler *et al.*[51]	Turkey	20	20	47·1(10)	49·5(14·2)	15 : 5	14 : 6	26·1(3·9)	27·8(3·6)	n.r.
Tsimogiannis *et al.*[29]	Greece	20	20	42·2(7·3)	48·5(12·8)	15 : 5	13 : 7	n.r.	n.r.	n.r.
Tsimoyiannis *et al.*[30]	Greece	20	20	49·2(16·9)	47·9(9·8)	15 : 5	19 : 1	n.r.	n.r.	n.r.
Vilallonga *et al.*[31]	Spain, Turkey	69	71	43·2(14·6)	42·6(14·6)	38 : 31	36 : 35	n.r.	n.r.	30
Yilmaz *et al.*[42]	Turkey	43	40	48·5(12)	51(9)	34 : 9	27 : 13	24·2(4)	23·3(3)	1
Zapf *et al.*[49]	USA	49	51	44·2(16·2)	50·9(18·2)	42 : 7	34 : 17	29·1(6·5)	30(6·3)	69
Zheng *et al.*[43]	China	30	30	43·6(11·3)	46·8(14·4)	17 : 13	14 : 16	24·7(3·4)	25·9(4·1)	48

*Values are mean(s.d.), except †median (i.q.r.). ‡Numbers as reported by Aprea *et al.*[32]. SILC, single-incision laparoscopic cholecystectomy; MLC, multiport laparoscopic cholecystectomy; n.r., not reported.

Included studies

The 37 trials included a total of 3051 patients, 1529 (50·1 per cent) in the SILC and 1522 (49·9 per cent) in the MLC group. One trial[16] had a 1·5 : 1 allocation ratio, with more patients in the SILC group. Another trial[17] allocated patients equally to four-port, three-port and single-port laparoscopic cholecystectomy; the four- and three-port groups were analysed as a single group, resulting in a 2 : 1 ratio. A third study[18] had a 2 : 1 allocation ratio with fewer patients in the MLC group. The remaining studies allocated in a 1 : 1 ratio. The mean(s.d.) age was 46·8(4·8) years in the SILC group and 48·0(5·7) years in the MLC group; 36 of 37 trials provided this information. The mean(s.d.) proportion of women was 67(3) per cent in the SILC group and 64(3) per cent in the MLC group. In only two trials[19,20] were more men than women included in both groups. Two trials[18,21] included only women and another four trials[22–25] did not provide this information. All except seven studies[23,26–31] reported BMI. The mean(s.d.) BMI was 26·6(2·1) kg/m² in the SILC group and 26·1(2·5) kg/m² in the MLC group. Twenty-one studies[16,17,19,21,23,24,28–30,32–43] excluded obese participants depending on the BMI. Twelve trials[17,18,26,29,30,32,34,35,37,44–46] included only patients with an ASA grade of I or II and nine[16,19–21,38,39,42,47,48] included only patients with ASA grade I–III. In 16 trials the anaesthetic risk status was not available. Only three trials[31,34,49] included emergency laparoscopic cholecystectomies.

Eight trials performed conventional cholecystectomy with three ports, 27 with four ports and two with both methods. In the SILC group, 17 trials[15,16,18–21,27,36,41,42,44–48,50,51] used the SILS™ Port Access System (Covidien, Mansfield, Massachusetts, USA), six[22,24,29,32,38,43] the TriPort™ Access System (Olympus, Center Valley, Pennsylvania, USA), two[23,25] the SITRAC® Access Device (Edlo, Porto Alegre, Brazil) and one[37] the QuadraPort® Access Device (Lagis, Taichung, Taiwan). One trial[31] used both the TriPort™ and SILS™ Port, and nine trials[17,26,30,33–35,39,40,49] did not use a particular access device. Information about the access device was not available in one trial[28]. Follow-up ranged between 1 and 69 weeks. Seven studies[26–30,32,51] did not report

Reference	SILC Score*	SILC *n*	MLC Score*	MLC *n*	Weight (%)	Mean difference
BIQ score at discharge						
Bucher *et al.*[22]	6(0·52)	75	8·51(1·05)	75	35·0	–2·51 (–2·77, –2·25)
Subtotal		75		75	35·0	–2·51 (–2·77, –2·25)
Heterogeneity: Not applicable						
Test for overall effect: $Z = 18{\cdot}62$, $P < 0{\cdot}001$						
BIQ score at 7–10 days						
Borle *et al.*[50]	6·23(0·89)	30	8·26(1·08)	30	28·9	–2·03 (–2·53, –1·53)
Bucher *et al.*[22]	5·51(0·53)	75	7·25(0·78)	75	36·1	–1·74 (–1·95, –1·53)
Subtotal		105		105	65·0	–1·79 (–2·01, –1·57)
Heterogeneity: $\tau^2 = 0{\cdot}00$; $\chi^2 = 1{\cdot}09$, 1 d.f., $P = 0{\cdot}30$; $I^2 = 8\%$						
Test for overall effect: $Z = 16{\cdot}01$, $P < 0{\cdot}001$						
Total		180		180	100·0	–2·09 (–2·64, –1·55)
Heterogeneity: $\tau^2 = 0{\cdot}20$; $\chi^2 = 19{\cdot}75$, 2 d.f., $P < 0{\cdot}001$; $I^2 = 90\%$						
Test for overall effect: $Z = 7{\cdot}53$, $P < 0{\cdot}001$						
Test for subgroup differences: $\chi^2 = 16{\cdot}75$, 1 d.f., $P < 0{\cdot}001$, $I^2 = 94{\cdot}0\%$						

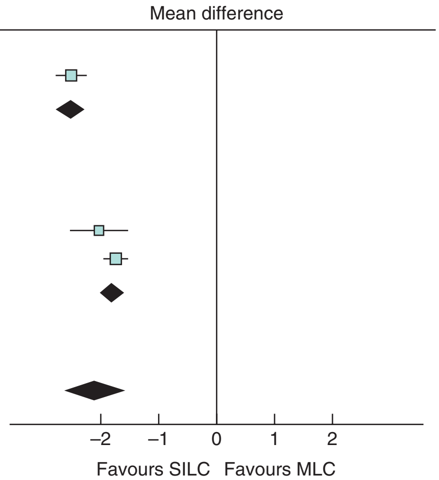

Fig. 2 Forest plot comparing short-term Body Image Questionnaire (BIQ) scores after single-incision (SILC) *versus* multiport (MLC) laparoscopic cholecystectomy. *Values are mean(s.d.). A random-effects inverse-variance model was used for meta-analysis. Mean differences are shown with 95 per cent confidence intervals

Reference	SILC Score*	SILC *n*	MLC Score*	MLC *n*	Weight (%)	Mean difference
BIQ score at 1 month						
Borle *et al.*[50]	5·5(0·68)	30	8(1·31)	30	28·3	–2·50 (–3·03, –1·97)
Bucher *et al.*[22]	5·25(0·27)	75	6(0·52)	75	36·2	–0·75 (–0·88, –0·62)
Subtotal		105		105	64·5	–1·61 (–3·32, 0·11)
Heterogeneity: $\tau^2 = 1{\cdot}49$; $\chi^2 = 39{\cdot}69$, 1 d.f., $P < 0{\cdot}001$; $I^2 = 97\%$						
Test for overall effect: $Z = 1{\cdot}84$, $P = 0{\cdot}07$						
BIQ score at 3 months						
Lurje *et al.*[15]	5(0·41)	48	6(0·53)	48	35·5	–1·00 (–1·19, –0·81)
Subtotal		48		48	35·5	–1·00 (–1·19, –0·81)
Heterogeneity: Not applicable						
Test for overall effect: $Z = 10{\cdot}33$, $P < 0{\cdot}001$						
Total		153		153	100·0	–1·33 (–1·92, –0·75)
Heterogeneity: $\tau^2 = 0{\cdot}24$; $\chi^2 = 41{\cdot}27$, 2 d.f., $P < 0{\cdot}001$; $I^2 = 95\%$						
Test for overall effect: $Z = 4{\cdot}49$, $P < 0{\cdot}001$						
Test for subgroup differences: $\chi^2 = 0{\cdot}47$, 1 d.f., $P = 0{\cdot}49$, $I^2 = 0\%$						

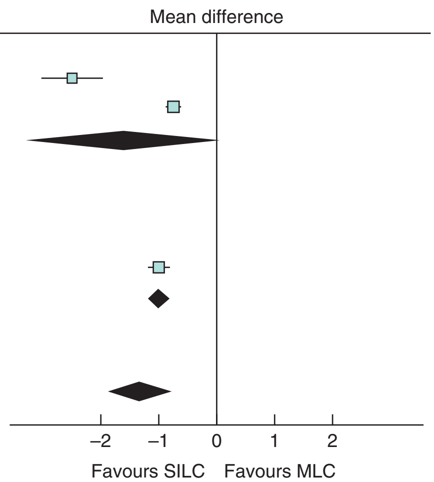

Fig. 3 Forest plot comparing mid-term Body Image Questionnaire (BIQ) scores after single-incision (SILC) *versus* multiport (MLC) laparoscopic cholecystectomy. *Values are mean(s.d.). A random-effects inverse-variance model was used for meta-analysis. Mean differences are shown with 95 per cent confidence intervals

Reference	SILC Score*	SILC n	MLC Score*	MLC n	Weight (%)	Mean difference
Cosmesis at 1 week						
Marks *et al.*[16]	20·5(3·6)	116	18·6(3·9)	80	32·0	1·90 (0.82, 2·98)
Borle *et al.*[50]	19·56(1·07)	30	15(1·2)	30	35·5	4·56 (3·98, 5·14)
Subtotal		146		110	67·6	3·27 (0·67, 5·88)
Heterogeneity: $\tau^2 = 3·34$; $\chi^2 = 18·24$, 1 d.f., $P < 0·001$; $I^2 = 95\%$						
Test for overall effect: $Z = 2·46$, $P = 0·01$						
Cosmesis at 2 weeks						
Marks *et al.*[16]	21·5(3·1)	115	18·5(3·9)	79	32·4	3·00 (1·97, 4·03)
Subtotal		115		79	32·4	3·00 (1·97, 4·03)
Heterogeneity: Not applicable						
Test for overall effect: $Z = 5·71$, $P < 0·001$						
Total		261		189	100·0	3·20 (1·55, 4·85)
Heterogeneity: $\tau^2 = 1·90$; $\chi^2 = 20·97$, 2 d.f., $P < 0·001$; $I^2 = 90\%$						
Test for overall effect: $Z = 3·81$, $P < 0·001$						
Test for subgroup differences: $\chi^2 = 0·04$, 1 d.f., $P = 0·85$, $I^2 = 0\%$						

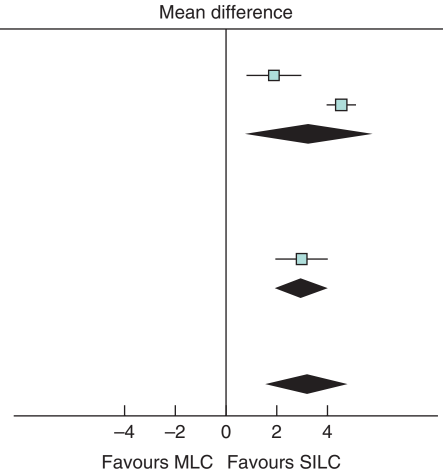

Fig. 4 Forest plot comparing short-term cosmesis scores after single-incision (SILC) *versus* multiport (MLC) laparoscopic cholecystectomy. *Values are mean(s.d.). A random-effects inverse-variance model was used for meta-analysis. Mean differences are shown with 95 per cent confidence intervals

Reference	SILC Score*	SILC n	MLC Score*	MLC n	Weight (%)	Mean difference
Cosmesis at 1 month						
Marks *et al.*[16]	22·1(2·7)	114	19·2(3·8)	76	23·6	2·90 (1·91, 3·89)
Borle *et al.*[50]	21·13(0·57)	30	15·63(1·06)	30	26·4	5·50 (5·07, 5·93)
Subtotal		144		106	50·0	4·24 (1·69, 6·79)
Heterogeneity: $\tau^2 = 3·23$; $\chi^2 = 22·37$, 1 d.f., $P < 0·001$; $I^2 = 96\%$						
Test for overall effect: $Z = 3·26$, $P = 0·001$						
Cosmesis at 3 months						
Marks *et al.*[16]	22·5(2·6)	110	20(3·3)	72	24·1	2·50 (1·60, 3·40)
Lurje *et al.*[15]	21(1·06)	48	16(1·59)	48	25·9	5·00 (4·46, 5·54)
Subtotal		158		120	50·0	3·78 (1·33, 6·23)
Heterogeneity: $\tau^2 = 2·98$; $\chi^2 = 21·62$, 1 d.f., $P < 0·001$; $I^2 = 95\%$						
Test for overall effect: $Z = 3·02$, $P = 0·003$						
Total		302		226	100·0	4·03 (2·70, 5·37)
Heterogeneity: $\tau^2 = 1·70$; $\chi^2 = 49·73$, 3 d.f., $P < 0·001$; $I^2 = 94\%$						
Test for overall effect: $Z = 5·93$, $P < 0·001$						
Test for subgroup differences: $\chi^2 = 0·07$, 1 d.f., $P = 0·80$, $I^2 = 0\%$						

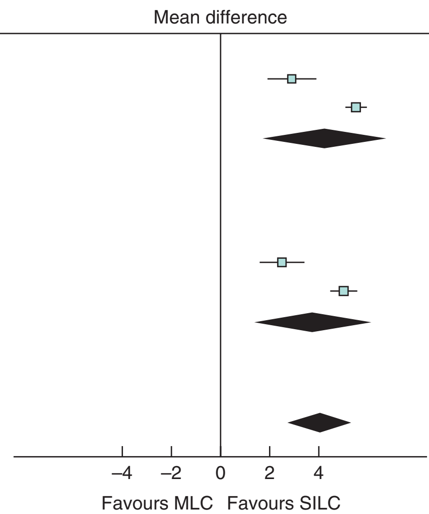

Fig. 5 Forest plot comparing mid-term cosmesis scores after single-incision (SILC) *versus* multiport (MLC) laparoscopic cholecystectomy. *Values are mean(s.d.). A random-effects inverse-variance model was used for meta-analysis. Mean differences are shown with 95 per cent confidence intervals

this information. Further details of included studies can be found in *Table 1* and *Appendix S1* (supporting information).

Excluded studies

Sixty-three studies were excluded after assessment of the full-text articles (*Appendix S1*, supporting information). Only abstracts were available for 41 studies. Six were not randomized trials or the control group was not MLC or SILC. In five trials the study population was the same as that in one of the included studies. Three articles were duplicate publications and in another three trials the participants were children. Two comments were excluded, and also two interim reports of included studies and one study protocol.

Risk of bias in included studies

The risk-of-bias assessment is described in detail in *Appendix S2* and summarized in *Fig. S1* (supporting information). Only three trials[15,19,21] had an overall low risk of bias.

Primary outcomes

Body image and cosmesis

The BIQ score measures the patient's perception of their body as well as their attitude towards their appearance[13]. Three trials[15,22,50] used this score. The values were recorded at different time points. Because of the small sample sizes, the data were pooled in short-term (1–14 days), mid-term (1–3 months) and long-term (6–12 months) groups. On pooling the data, statistically significant differences were found in favour of SILC in the short- and mid-term groups. There was significant heterogeneity in the short-term ($I^2 = 90$ per cent, $P < 0·001$) and mid-term ($I^2 = 95$ per cent, $P < 0·001$) groups. In the random-effects model, the mean BIQ score was lower for patients who had SILC, indicating a better perception of their body in the short term (MD −2·09, 95 per cent c.i. −2·64 to −1·55; $P < 0·001$) (*Fig. 2*). Similarly, in the random-effects model, the mean BIQ score was lower in the mid term for patients who underwent SILC (MD −1·33, −1·92 to −0·75; $P < 0·001$) (*Fig. 3*). Only one study[15] reported the BIQ score after 1 year. At this time, the score was superior in the SILC group compared with the MLC group (5 *versus* 6; $P = 0·017$).

Reference	SILC Score*	SILC *n*	MLC Score*	MLC *n*	Weight (%)	Mean difference
Marks *et al.*[16]	22·6(2·4)	99	20·2(3·7)	62	49·6	2·40 (1·36, 3·44)
Lurje *et al.*[15]	23·49(0·55)	48	16·2(1·86)	48	50·4	7·29 (6·74, 7·84)
Total		147		110	100·0	4·87 (0·07, 9·66)

Heterogeneity: $\tau^2 = 11·78$; $\chi^2 = 66·97$, 1 d.f., $P < 0·001$; $I^2 = 99\%$
Test for overall effect: $Z = 1·99$, $P = 0·05$

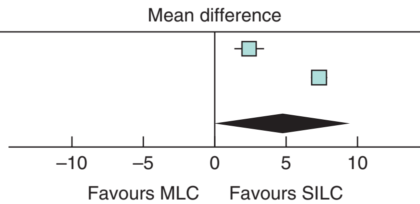

Fig. 6 Forest plot comparing long-term cosmesis scores after single-incision (SILC) *versus* multiport (MLC) laparoscopic cholecystectomy. *Values are mean(s.d.). A random-effects inverse-variance model was used for meta-analysis. Mean differences are shown with 95 per cent confidence intervals

Reference	SILC Score*	SILC *n*	MLC Score*	MLC *n*	Weight (%)	Mean difference
Wound satisfaction at discharge						
Sasaki *et al.*[20]	9·7(0·5)	27	8·9(1·2)	27	21·2	0·80 (0·31, 1·29)
Lirici *et al.*[38]	8·24(1·45)	20	6·43(2·93)	20	16·1	1·81 (0·43, 3·19)
Subtotal		47		47	37·4	1·09 (0·19, 1·99)
Heterogeneity: $\tau^2 = 0·23$; $\chi^2 = 1·83$, 1 d.f., $P = 0·18$; $I^2 = 45\%$						
Test for overall effect: $Z = 2·39$, $P = 0·02$						
Wound satisfaction at 7–14 days						
Saad *et al.*[19]	8·7(2·36)	35	8·86(1·22)	35	19·3	–0·16 (–1·04, 0·72)
Sasaki *et al.*[20]	9·9(0·2)	27	9·2(0·8)	27	21·8	0·70 (0·39, 1·01)
Aprea *et al.*[32]	9·8(0·4)	25	7(1)	25	21·5	2·80 (2·38, 3·22)
Subtotal		87		87	62·6	1·14 (–0·51, 2·79)
Heterogeneity: $\tau^2 = 2·04$; $\chi^2 = 73·33$, 2 d.f., $P < 0·001$; $I^2 = 97\%$						
Test for overall effect: $Z = 1·36$, $P = 0·17$						
Total		134		134	100·0	1·19 (0·13, 2·24)

Heterogeneity: $\tau^2 = 1·30$; $\chi^2 = 77·49$, 4 d.f., $P < 0·001$; $I^2 = 95\%$
Test for overall effect: $Z = 2·21$, $P = 0·03$
Test for subgroup differences: $\chi^2 = 0·00$, 1 d.f., $P = 0·96$, $I^2 = 0\%$

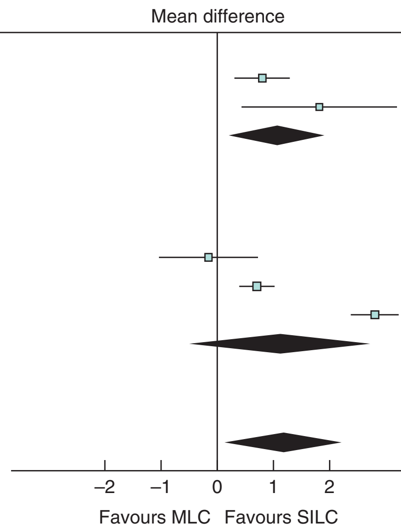

Fig. 7 Forest plot comparing short-term wound satisfaction scores after single-incision (SILC) *versus* multiport (MLC) laparoscopic cholecystectomy. *Values are mean(s.d.). A random-effects inverse-variance model was used for meta-analysis. Mean differences are shown with 95 per cent confidence intervals

Cosmesis score is the degree of patient satisfaction with respect to appearance of scar(s)[13]. Three trials[15,16,50] used this score. The values were recorded at different time points. Again, the data were pooled in short-term (1–14 days), mid-term (1–3 months) and long-term (6–12 months) groups. On pooling the data, statistically significant differences were found in favour of SILC in all intervals. There was significant heterogeneity in the short-term ($I^2 = 90$ per cent, $P < 0{\cdot}001$), mid-term ($I^2 = 94$ per cent, $P < 0{\cdot}001$) and long-term ($I^2 = 99$ per cent, $P < 0{\cdot}001$) groups. In the random-effects model, in the short term (MD 3·20, 1·55 to 4·85; $P < 0{\cdot}001$) (*Fig. 4*), mid term (MD 4·03, 2·70 to 5·37; $P < 0{\cdot}001$) (*Fig. 5*) and long term (MD 4·87, 0·07 to 9·66; $P = 0{\cdot}05$) (*Fig. 6*), the mean cosmesis score was higher among patients who had SILC, indicating better satisfaction with the scar(s).

Wound satisfaction score

In 12 trials[17,19–21,31,32,35,37–39,47,48] satisfaction with the wound was assessed on a scale from 1 to 10, analogous to the well known VAS used for pain assessment. The values were recorded at different time points. The data were pooled in short-term (1–14 days), mid-term (1–3 months) and long-term (6–12 months) groups. On pooling the data, statistically significant differences were found in favour of SILC in all three intervals. There was significant heterogeneity in the short-term ($I^2 = 95$ per cent, $P < 0{\cdot}001$), mid-term ($I^2 = 98$ per cent, $P < 0{\cdot}001$) and long-term ($I^2 = 98$ per cent, $P < 0{\cdot}001$) groups. In the random-effects model, in the short term (MD 1·19, 95 per cent c.i. 0·13 to 2·24; $P = 0{\cdot}03$) (*Fig. 7*), mid term (MD 1·38, 0·63 to 2·14; $P < 0{\cdot}001$) (*Fig. 8*) and long term (MD 1·19, 0·18 to 2·20; $P = 0{\cdot}02$) (*Fig. 9*), the mean wound satisfaction score was higher in patients who underwent SILC, indicating greater satisfaction with the wound(s).

Secondary outcomes

An overview of the secondary outcomes is provided in *Table 2*.

	SILC		MLC			
Reference	Score*	*n*	Score*	*n*	Weight (%)	Mean difference
Wound satisfaction at 1 month						
Abd Ellatif *et al.*[35]	8·2(1·2)	125	7·3(1·6)	125	11·6	0·90 (0·55, 1·25)
Lee *et al.*[37]	8·7(1)	35	7·7(1·4)	35	11·1	1·00 (0·43, 1·57)
Vilallonga *et al.*[31]	8·8(0·9)	69	7·5(1·3)	71	11·6	1·30 (0·93, 1·67)
Lirici *et al.*[38]	9·21(0·91)	20	6·9(2·97)	20	8·6	2·31 (0·95, 3·67)
Jørgensen *et al.*[21]	8·49(1·06)	60	5(0·53)	60	11·7	3·49 (3·19, 3·79)
Subtotal		309		311	54·6	1·79 (0·56, 3·02)
Heterogeneity: $\tau^2 = 1{\cdot}85$; $\chi^2 = 159{\cdot}39$, 4 d.f., $P < 0{\cdot}001$; $I^2 = 97\%$						
Test for overall effect: $Z = 2{\cdot}85$, $P = 0{\cdot}004$						
Wound satisfaction at 2 months						
Pan *et al.*[39]	8(0·4)	49	6(0.2)	53	11·9	2·00 (1·88, 2·12)
Subtotal		49		53	11·9	2·00 (1·88, 2·12)
Heterogeneity: Not applicable						
Test for overall effect: $Z = 31{\cdot}54$, $P < 0{\cdot}001$						
Wound satisfaction at 3 months						
Khorgami *et al.*[17]	9·9(0·3)	30	9·6(0·55)	60	11·8	0·30 (0·12, 0·48)
Saad *et al.*[19]	9·4(1·18)	35	8·88(1·64)	35	10·9	0·52 (–0·15, 1·19)
Lai *et al.*[48]	6·48(1·14)	24	5·74(1·39)	27	10·8	0·74 (0·05, 1·43)
Subtotal		89		122	33·5	0·34 (0·17, 0·50)
Heterogeneity: $\tau^2 = 0{\cdot}00$; $\chi^2 = 1{\cdot}75$, 2 d.f., $P = 0{\cdot}42$; $I^2 = 0\%$						
Test for overall effect: $Z = 4{\cdot}02$, $P < 0{\cdot}001$						
Total		447		486	100·0	1·38 (0·63, 2·14)
Heterogeneity: $\tau^2 = 1{\cdot}25$; $\chi^2 = 441{\cdot}00$, 8 d.f., $P < 0{\cdot}001$; $I^2 = 98\%$						
Test for overall effect: $Z = 3{\cdot}58$, $P < 0{\cdot}001$						
Test for subgroup differences: $\chi^2 = 248{\cdot}76$, 2 d.f., $P < 0{\cdot}001$, $I^2 = 99{\cdot}2\%$						

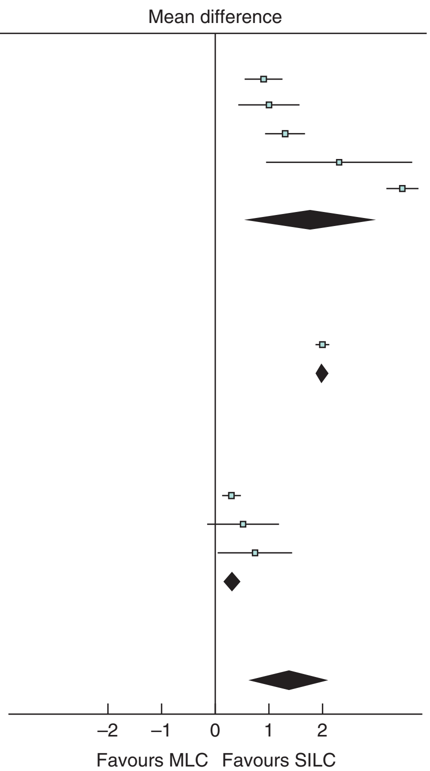

Fig. 8 Forest plot comparing mid-term wound satisfaction scores after single-incision (SILC) *versus* multiport (MLC) laparoscopic cholecystectomy. *Values are mean(s.d.). A random-effects inverse-variance model was used for meta-analysis. Mean differences are shown with 95 per cent confidence intervals

Reference	SILC Score*	SILC *n*	MLC Score*	MLC *n*	Weight (%)	Mean difference
Wound satisfaction at 6 months						
Saad *et al.*[19]	9·7(0·72)	35	9·08(1·48)	35	14·2	0·62 (0·07, 1·17)
Lee *et al.*[37]	9·1(1)	35	8·4(1·1)	35	14·3	0·70 (0·21, 1·19)
Abd Ellatif *et al.*[35]	9·7(2·5)	125	8·5(1·6)	125	14·2	1·20 (0·68, 1·72)
Deveci *et al.*[47]	8·56(2·12)	50	6·6(1·86)	50	13·6	1·96 (1·18, 2·74)
Subtotal		245		245	56·3	1·06 (0·55, 1·57)
Heterogeneity: $\tau^2 = 0·19$; $\chi^2 = 9·64$, 3 d.f., $P = 0·02$; $I^2 = 69\%$						
Test for overall effect: $Z = 4·07$, $P < 0·001$						
Wound satisfaction at 1 year						
Saad *et al.*[19]	9·82(0·6)	35	9·76(0·82)	35	14·6	0·06 (–0·28, 0·40)
Khorgami *et al.*[17]	9·7(0·5)	30	9·6(0·55)	60	14·7	0·10 (–0·13, 0·33)
Jørgensen *et al.*[21]	8·49(1·06)	60	4·75(1·31)	60	14·4	3·74 (3·31, 4·17)
Subtotal		125		155	43·7	1·29 (–0·72, 3·31)
Heterogeneity: $\tau^2 = 3·14$; $\chi^2 = 235·88$, 2 d.f., $P < 0·001$; $I^2 = 99\%$						
Test for overall effect: $Z = 1·26$, $P = 0·21$						
Total		370		400	100·0	1·19 (0·18, 2·20)
Heterogeneity: $\tau^2 = 1·80$; $\chi^2 = 248·78$, 6 d.f., $P < 0·001$; $I^2 = 98\%$						
Test for overall effect: $Z = 2·30$, $P = 0·02$						
Test for subgroup differences: $\chi^2 = 0·05$, 1 d.f., $P = 0·83$, $I^2 = 0\%$						

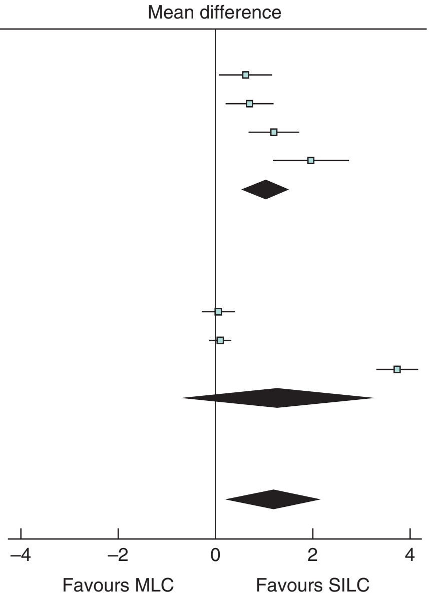

Fig. 9 Forest plot comparing long-term wound satisfaction scores after single-incision (SILC) *versus* multiport (MLC) laparoscopic cholecystectomy. *Values are mean(s.d.). A random-effects inverse-variance model was used for meta-analysis. Mean differences are shown with 95 per cent confidence intervals

Intraoperative outcomes

Thirteen trials reported intraoperative blood loss. There was significant heterogeneity among the trials ($I^2 = 62$ per cent, $P = 0·002$). In the random-effects model, mean intraoperative blood loss was similar for both groups (MD −0·08 (95 per cent c.i. −1·83 to 1·68) ml; $P = 0·93$) (*Fig. S2*, supporting information).

Twenty-nine trials reported the duration of operation. There was significant heterogeneity among the trials ($I^2 = 91$ per cent, $P < 0·001$). In the random-effects model, the mean time taken to perform SILC was 13·56 min longer than that for MLC (MD 13·56 (95 per cent c.i. 10·02 to 17·09) min; $P < 0·001$) (*Fig. 10*).

Thirty-one trials reported whether an additional trocar was necessary to complete surgery. In four trials an additional trocar was not necessary in either group. A total of six additional trocars were used in the MLC groups, four in operations starting as three-port and two in procedures starting as four-port laparoscopic cholecystectomy. Ninety additional trocars were used to complete cholecystectomy in the SILC groups. There was no heterogeneity among the 27 trials included in the meta-analysis ($I^2 = 0$ per cent, $P = 0·92$). In the fixed-effect model, additional ports were more often required to perform SILC than MLC (OR 6·78, 95 per cent c.i. 4·08 to 11·26; $P < 0·001$) (*Fig. S3*, supporting information).

Thirty-three trials reported the rate of conversion to open surgery. Seven laparoscopic cholecystectomies were converted in the SILC group and ten in the MLC group. There was no heterogeneity among the six trials included in the meta-analysis ($I^2 = 0$ per cent, $P = 0·94$). In the fixed-effect model, the conversion rate was similar for both groups (OR 0·71, 95 per cent c.i. 0·29 to 1·78; $P = 0·47$) (*Fig. S4*, supporting information).

Postoperative outcomes

Only seven[16,24,29,40,46,49,50] trials did not report postoperative pain at least at one time point. Pain scores measured on a VAS were obtained at ten time points (3, 4, 8, 12, 24, 48 and 72 h, 7 and 14 days, and 1 month). There was significant heterogeneity at all time points ($I^2 = 62–95$ per cent). There was a slight trend towards less postoperative pain for SILC at most time points, but this was only significant after 12 h (*Table 3*; *Figs S5–S14*, supporting information). In the random-effects model, the mean postoperative pain score after 12 h was higher in the MLC group (MD −0·80, 95 per cent c.i. −1·39 to −0·22; $P = 0·007$), whereas after 7 days there was a slight trend towards less postoperative pain among patients who had MLC (MD 0·11, −0·54 to 0·77; $P = 0·74$).

Twenty-four trials reported the length of hospital stay There was significant heterogeneity among the trials

Table 2 Overview of secondary outcomes

	No. of studies	No. of events or *mean SILC	MLC	Odds ratio or †mean difference	P	I^2 (%)
Intraoperative blood loss (ml)	13	15·88*	17·33*	−0·08 (−1·83, 1·68)†	0·93	62
Duration of operation (min)	29	67·11*	51·91*	13·56 (10·02, 17·09)†	< 0·001	91
Use of additional ports	27	90	6	6·78 (4·08, 11·26)	< 0·001	0
Conversion to open surgery	6	7	10	0·71 (0·29, 1·78)	0·47	0
Length of hospital stay (days)	24	1·79*	1·86*	−0·05 (−0·14, 0·04)†	0·32	86
Time to return to work (days)	9	8·36*	8·87*	−0·72 (−1·60, 0·15)†	0·10	86
Gallbladder perforation	7	33	28	1·33 (0·78, 2·28)	0·29	0
Retained bile duct stones	5	6	2	2·03 (0·57, 7·27)	0·28	0
Bile leakage	6	5	3	1·25 (0·41, 3·80)	0·69	0
Intraoperative bleeding	7	8	11	0·84 (0·36, 1·94)	0·68	0
Haematoma	4	7	7	1·02 (0·37, 2·86)	0·97	0
Seroma	5	7	8	0·86 (0·32, 2·28)	0·76	0
Pneumothorax	3	3	0	3·10 (0·48, 20·13)	0·24	0
Port-site hernia	10	19	5	2·50 (1·10, 5·69)	0·03	0

Values in parentheses are 95 per cent confidence intervals. SILC, single-incision laparoscopic cholecystectomy; MLC, multiport laparoscopic cholecystectomy.

($I^2 = 86$ per cent, $P < 0{\cdot}001$). In the random-effects model, the mean stay was similar in both groups (MD −0·05 (95 per cent c.i. −0·14 to 0·04) days; $P = 0{\cdot}32$) (*Fig. S15*, supporting information).

Time to return to work was reported in nine trials. There was significant heterogeneity among the trials ($I^2 = 86$ per cent, $P < 0{\cdot}001$). In the random-effects model, the mean time to return to work was similar in the two groups (MD −0·72 (−1·60 to 0·15) days; $P = 0{\cdot}10$) (*Fig. S16*, supporting information).

Complications

Gallbladder perforation or bile spillage was reported in seven trials. There was no heterogeneity among the trials ($I^2 = 0$ per cent, $P = 0{\cdot}64$). In the fixed-effect model, the frequency of gallbladder perforation or bile spillage was similar for both groups (OR 1·33, 95 per cent c.i. 0·78 to 2·28; $P = 0{\cdot}29$) (*Fig. S17*, supporting information).

Retained bile duct stones that required postoperative endoscopic retrograde cholangiopancreatography were reported in seven trials. There was no heterogeneity among the five trials included in the meta-analysis ($I^2 = 0$ per cent, $P = 0{\cdot}94$). In the fixed-effect model, the frequency of retained bile duct stones was similar for both groups, with a trend towards more stones after SILC (OR 2·03, 0·57 to 7·27; $P = 0{\cdot}28$) (*Fig. S18*, supporting information).

Postoperative bile leakage was reported in eight trials. There was no heterogeneity among the six trials included in the meta-analysis ($I^2 = 0$ per cent, $P = 0{\cdot}74$). The fixed-effect model showed that the frequency of postoperative bile leakage was similar after both procedures (OR 1·25, 0·41 to 3·80; $P = 0{\cdot}69$) (*Fig. S19*, supporting information). Only Lirici *et al.*[38] reported one recognized intraoperative bile duct injury (BDI), a partial avulsion of a short cystic duct from the common bile duct in the MLC group. This complication required conversion to open surgery for safe repair.

Sixteen trials[15,19–24,26,30,32,33,35,41,45,47,49] reported whether intraoperative cholangiography (IOC) was undertaken. In these 16 studies, only 94 cholangiograms were performed in 658 SILC operations, and 105 cholangiograms in 670 MLCs. Eight of these 16 trials did not undertake cholangiography, and only two studies[22,26] reported performing IOC routinely. There was no heterogeneity among the seven trials included in the meta-analysis ($I^2 = 0$ per cent, $P = 0{\cdot}89$). In the fixed-effect model, cholangiography was used in a similar proportion of procedures in both groups (OR 0·90, 0·52 to 1·54; $P = 0{\cdot}70$) (*Fig. S20*, supporting information).

Relevant intraoperative bleeding was reported in seven trials. There was no heterogeneity among the trials ($I^2 = 0$ per cent, $P = 0{\cdot}56$). The fixed-effect model showed no difference between the groups in the frequency of relevant intraoperative bleeding (OR 0·84, 0·36 to 1·94; $P = 0{\cdot}68$) (*Fig. S21*, supporting information).

Postoperative haematoma was reported in four trials. There was no heterogeneity among the trials ($I^2 = 0$ per cent, $P = 0{\cdot}70$). In the fixed-effect model, the frequency of haematoma was similar for both groups (OR 1·02, 0·37 to 2·86; $P = 0{\cdot}97$) (*Fig. S22*, supporting information).

Postoperative seroma was reported in five trials. There was no heterogeneity among the trials ($I^2 = 0$ per cent, $P = 0{\cdot}87$). There was no difference between the groups in

	SILC		MLC			
Reference	Time (min)*	*n*	Time (min)*	*n*	Weight (%)	Mean difference (min)
Lirici *et al.*[38]	77·63(20·1)	20	94·06(79·16)	20	0·8	−16·43 (−52·22, 19·36)
Yilmaz *et al.*[42]	34·6(15)	43	39·3(11)	40	4·1	−4·70 (−10·33, 0·93)
Lai *et al.*[48]	43·5(15·4)	24	46·5(20·1)	27	3·4	−3·00 (−12·77, 6·77)
Bucher *et al.*[22]	68·28(20·02)	75	70·84(20·58)	75	3·9	−2·56 (−9·06, 3·94)
Rašić *et al.*[40]	46(3·5)	48	43(4)	50	4·5	3·00 (1·51, 4·49)
Pan *et al.*[39]	41·8(17)	49	38·5(22)	53	3·7	3·30 (−4·30, 10·90)
Vilallonga *et al.*[31]	63·9(20·3)	69	58·4(20·8)	71	3·9	5·50 (−1·31, 12·31)
Herrero Fonollosa *et al.*[36]	54(21)	26	48·5(17)	24	3·2	5·50 (−5·06, 16·06)
Aprea *et al.*[32]	41·3(12)	25	35·6(5·8)	25	4·1	5·70 (0·48, 10·92)
Solomon *et al.*[18]	48·9(2·6)	22	42·3(3·9)	11	4·4	6·60 (4·05, 9·15)
Abd Ellatif *et al.*[35]	62·7(10·2)	125	55·3(8·9)	125	4·4	7·40 (5·03, 9·77)
Cao *et al.*[34]	55·2(12·4)	57	46·3(10·8)	51	4·2	8·90 (4·52, 13·28)
Bresadola *et al.*[26]	94(29)	28	85(33)	37	2·5	9·00 (−6·11, 24·11)
Khorgami *et al.*[17]	63·7(9·8)	30	53·6(13·95)	60	4·2	10·10 (5·12, 15·08)
Saad *et al.*[19]	45·7(10·9)	35	35(14)	35	4·0	10·70 (4·82, 16·58)
Lurje *et al.*[15]	101(36)	48	90(41)	48	2·4	11·00 (−4·44, 26·44)
Tsimoyiannis *et al.*[30]	49·64(9·02)	20	37·3(9·16)	20	4·1	12·34 (6·71, 17·97)
Zheng *et al.*[43]	55·6(25·7)	30	42·7(18·6)	30	3·1	12·90 (1·55, 24·25)
Sasaki *et al.*[20]	83·4(18·6)	27	69·4(16·7)	27	3·4	14·00 (4·57, 23·43)
Justo-Janeiro *et al.*[45]	67(21·9)	18	48·9(17·8)	19	2·8	18·10 (5·20, 31·00)
Brown *et al.*[33]	69·3(31·86)	40	50·85(16·44)	39	3·1	18·45 (7·31, 29·59)
Zapf *et al.*[49]	63·5(21)	49	43·8(24·2)	51	3·5	19·70 (10·83, 28·57)
Borle *et al.*[50]	69·53(8·96)	30	47·73(5·57)	30	4·3	21·80 (18·02, 25·58)
Lee *et al.*[37]	71·7(11·6)	35	48·4(10·5)	35	4·1	23·30 (18·12, 28·48)
Deveci *et al.*[47]	73(32·65)	50	48(15·08)	50	3·3	25·00 (15·03, 34·97)
Mehmood *et al.*[27]	80·17(30·16)	30	38·5(8·92)	30	3·1	41·67 (30·42, 52·92)
Telciler *et al.*[51]	96(31·14)	20	51·75(14·35)	20	2·5	44·25 (29·22, 59·28)
Luna *et al.*[23]	92(27·7)	20	41·9(14)	20	2·7	50·10 (36·50, 63·70)
Sinan *et al.*[41]	124·4(29·7)	17	64·1(26·1)	17	2·0	60·30 (41·50, 79·10)
Total		1110		1140	100·0	13·56 (10·02, 17·09)

Heterogeneity: $\tau^2 = 71·88$; $\chi^2 = 321·85$, 28 d.f., $P < 0·001$; $I^2 = 91\%$
Test for overall effect: $Z = 7·51$, $P < 0·001$

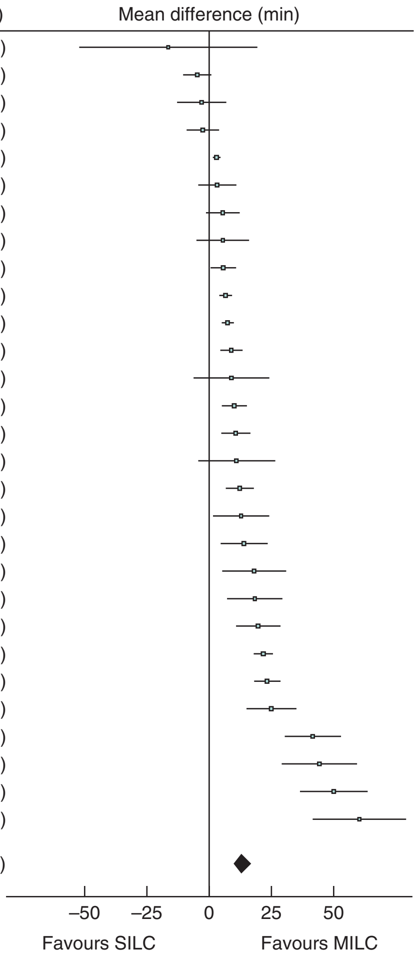

Fig. 10 Forest plot comparing duration of surgery for single-incision (SILC) *versus* multiport (MLC) laparoscopic cholecystectomy. *Values are mean(s.d.). A random-effects inverse-variance model was used for meta-analysis. Mean differences are shown with 95 per cent confidence intervals

the frequency of seroma (OR 0·86, 0·32 to 2·28; $P = 0·76$) (*Fig. S23*, supporting information).

Wound infection was reported in 15 trials. There was no heterogeneity among the trials ($I^2 = 0$ per cent, $P = 0·93$). In the fixed-effect model, the frequency of wound infection was similar after SILC and MLC (OR 1·23, 0·70 to 2·14; $P = 0·47$) (*Fig. S24*, supporting information).

Postoperative pneumothorax was reported in three trials. There was no heterogeneity among the trials ($I^2 = 0$ per cent, $P = 1·00$). The frequency of postoperative pneumothorax was similar for both groups in the fixed-effect model (OR 3·10, 0·48 to 20·13; $P = 0·24$) (*Fig. S25*, supporting information).

Port-site hernia was reported in ten trials including 927 patients (472 SILC, 455 MLC). There was no heterogeneity among the trials ($I^2 = 0$ per cent, $P = 0·90$). In the fixed-effect model, the frequency of port-site hernia was 19 of 472 (4·0 per cent) in the SILC group compared with five of 455 (1·1 per cent) in the MLC group (OR 2·50, 1·10 to 5·69; $P = 0·03$) (*Fig. 11*). The mean follow-up ranged from 4 to 69 weeks.

Postoperative use of analgesics

Twenty-four studies reported postoperative use of analgesics in the first 24 h. A meta-analysis was not undertaken because the initial pain therapy differed greatly among the

Table 3 Postoperative pain

Time after surgery	No. of studies	Mean VAS score		Mean difference	*P*	I^2 (%)
		SILC	MLC			
3 h	12	3·51	3·88	−0·34 (−0·86, 0·17)	0·19	62
4 h	8	3·64	4·15	−0·56 (−1·45, 0·33)	0·21	89
8 h	14	3·28	3·70	−0·43 (−1·12, 0·25)	0·21	93
12 h	9	2·63	3·40	−0·80 (−1·39, −0·22)	0·007	88
24 h	22	2·39	2·58	−0·20 (−0·59, 0·19)	0·31	92
48 h	8	1·42	1·91	−0·55 (−1·13, 0·04)	0·07	93
72 h	6	1·58	1·70	−0·12 (−0·74, 0·50)	0·71	95
7 days	5	1·28	1·89	0·11 (−0·54, 0·77)	0·74	88
14 days	3	0·98	1·30	−0·33 (−0·81, 0·16)	0·19	91
1 month	4	1·28	1·25	−0·16 (−0·52, 0·19)	0·37	82

Values in parentheses are 95 per cent confidence intervals. VAS, visual analogue scale; SILC, single-incision laparoscopic cholecystectomy; MLC, multiport laparoscopic cholecystectomy.

studies, and analgesics on demand also differed in substance and dose. In six studies[15,17,22,26,30,35], patients in the MLC group required significantly more pain relief in the first 24 h. In the remaining 18 studies, there was no significant difference between the two groups in the first 24 h.

Three studies[15,30,35] reported significantly greater consumption of analgesics more than 24 h after surgery in the MLC group. In the remaining studies, there was no difference between the two groups after 24 h.

Costs

Five studies reported the costs of the procedure or the whole hospital stay. A meta-analysis was not performed because the costs are specific to each country. Two studies[22,49] reported significantly higher costs for SILC. In the remaining three studies[33,39,46], the costs were similar for the two procedures.

Postoperative quality of life

Nine studies reported postoperative QoL. The authors used different questionnaires at multiple time points, and a meta-analysis was not therefore possible.

Brown *et al.*[33] used the Gastrointestinal Quality of Life Index (GIQLI) before surgery, and after 2 and 4 weeks. There was no difference statistically between the two groups at any time point. Saad *et al.*[19] used the GIQLI after 10 days and reported no difference between the two groups.

Bucher and colleagues[22] used the Short Form (SF) 12 (SF-12®; RAND Health Communications, Santa Monica, California, USA) before operation and after 4 weeks. There was no difference between the two groups before operation, but after 4 weeks QoL was significantly better in the SILC group.

Abd Ellatif and co-workers[35] used the EQ-5D™ (EuroQoL Group, Rotterdam, The Netherlands) before, and 1 week, 1 month and 6 months after surgery. There was no significant difference between the two groups at any time point.

Lirici *et al.*[38] used SF-36® after 1 month and reported no difference between the two groups. Lurje and colleagues[15] used SF-36® before operation, after 3 months and after 1 year. Before operation and after 3 months there was statistically no difference between the two groups. After 1 year, QoL was significantly better in the SILC group than in the MLC group with regard to emotional well-being, physical pain, physical health and mental health. Ma *et al.*[24] found no difference between the two groups in SF-36® scores before surgery and after 2–3 weeks.

Marks and co-workers[16] used SF-8® before operation, and after 1, 3, 5 and 7 days. They used SF-12® after 2 weeks and 1 month. Physical QoL scores favoured MLC over SILC statistically on day 3, after 1 week and 1 month, with no difference at other time points. Mental QoL scores were no different between the two groups.

Zapf and colleagues[49] used the Surgical Outcomes Measurement System before surgery, after 1 and 3 days, 1 and 3 weeks, 1 month, and 1 and 2 years. QoL showed a statistically similar postoperative course between the two groups in five of six outcome measures: physical and bowel function, fatigue, cosmesis and overall satisfaction at all time points. One outcome measure (impact of pain) favoured MLC over SILC before operation and on day 1 after surgery.

Difficulty in performing procedures

Three studies[15,19,38] reported difficulties in performing one of these techniques compared with the other. In the study of Lurje *et al.*[15], surgeons complained of discomfort in a

Reference	Port-site hernia SILC	Port-site hernia MLC	Weight (%)	Odds ratio
Vilallonga *et al.*[31]	1 of 69	2 of 71	24·3	0·51 (0·04, 5·73)
Khorgami *et al.*[17]	0 of 30	1 of 60	12·5	0·65 (0·03, 16·44)
Jørgensen *et al.*[21]	1 of 60	1 of 60	12·3	1·00 (0·06, 16·37)
Solomon *et al.*[18]	1 of 22	0 of 11	7·7	1·60 (0·06, 42·63)
Chang *et al.*[44]	1 of 51	0 of 50	6·1	3·00 (0·12, 75·41)
Saad *et al.*[19]	1 of 35	0 of 35	6·0	3·09 (0·12, 78·41)
Sinan *et al.*[41]	1 of 17	0 of 17	5·7	3·18 (0·12, 83·76)
Ma *et al.*[24]	1 of 21	0 of 22	5·7	3·29 (0·13, 85·44)
Lurje *et al.*[15]	2 of 48	0 of 48	5·9	5·22 (0·24, 111·55)
Marks *et al.*[16]	10 of 119	1 of 81	13·7	7·34 (0·92, 58·50)
Total	19 of 472	5 of 455	100·0	2·50 (1·10, 5·69)

Heterogeneity: $\chi^2 = 4{\cdot}15$, 9 d.f., $P = 0{\cdot}90$; $I^2 = 0\%$
Test for overall effect: $Z = 2{\cdot}19$, $P = 0{\cdot}03$

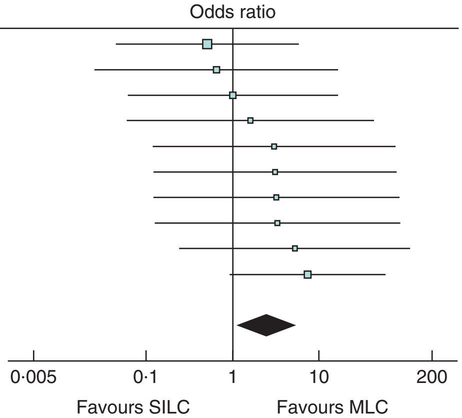

Fig. 11 Forest plot comparing rate of port-site hernia after single-incision (SILC) *versus* multiport (MLC) laparoscopic cholecystectomy. A Mantel–Haenszel fixed-effect model was used for meta-analysis. Odds ratios are shown with 95 per cent confidence intervals

significantly higher proportion of SILC procedures than MLC operations (12 of 48 *versus* 1 of 48 respectively).

Saad and co-workers[19] reported surgeons' ratings of the handling of instruments and camera, and preparation and gallbladder retrieval on a scale from 1 (very easy) to 5 (very difficult). Instrument and laparoscope handling was significantly better with the MLC than the SILC technique. Removal of the gallbladder from the abdomen was significantly easier in the SILC group. There was no difference in preparation.

Lirici and colleagues[38] scored difficulty of exposure and dissection on a scale from 1 (no difficulties) to 4 (most difficult). Exposure was significantly more difficult with SILC than MLC (mean score 1·5 (median 1, range 1–4) *versus* 2·2 (2, 1–3); $P = 0{\cdot}004$). The difficulty of dissection was similar for both groups.

Subgroup analysis

A subgroup analysis of the three trials[15,19,21] with an overall low risk of bias was performed. It showed two differences compared with the overall analysis. In the fixed-effect model, the postoperative pain score after 3 h was significantly higher after MLC (MD −0·97, 95 per cent c.i. −1·58 to −0·36; $P = 0{\cdot}002$); there was no heterogeneity among the trials. In addition, there was no significant difference between the two groups in terms of port-site hernia (OR 2·55, 95 per cent c.i. 0·49 to 13·32; $P = 0{\cdot}27$).

Discussion

This systematic review and meta-analysis found SILC to be associated with moderately, but statistically significantly better aesthetic results than MLC, as evaluated by the body image score and a linear score. This was shown not only for the early postoperative course, but also in mid- and long-term follow-up. Similarly, scar satisfaction, as evaluated by the cosmesis score, showed that patient satisfaction with the scar was significantly greater in the SILC group for all three time intervals evaluated. A clinically relevant improvement in body image and cosmesis scores is defined as an improvement of 20 per cent[13]. In the present study, the difference in body image scores between the SILC and MLC groups ranged between 8·8 and 16·7 per cent, indicating a moderate clinical benefit, whereas the cosmesis score showed an increase of 15·2–23·2 per cent in the SILC group, indicating a clinically moderate to significant improvement. Better cosmesis is one of the most frequently mentioned advantages of SILC. Although cosmesis is an important factor in body image-conscious patients, it has been claimed that, for the majority, cosmesis may be of less concern than surgeon reputation and avoidance of surgical complications[52]. Furthermore, after 21 months' follow-up, more than half of the patients who underwent MLC did not seem to remember the number of incisions they had[53]. It has also been noted that the incision experienced as the most painful, and that would therefore preferably be omitted by more than half of patients, is the umbilical type (as used as the single port in SILC)[54].

The overall published incidence of port-site hernia in MLC is stated to be 1·7 per cent[55]. The present study showed a significantly higher incidence of port-site hernia in the SILC group (4·0 per cent) compared with the MLC group (1·1 per cent) in a follow-up ranging from 1 to 17 months after surgery. Although a previous study[56] showed little difference between the two techniques, recent systematic reviews[9,11] have also shown a higher risk of port-site hernia with SILC. In the present review, one of the RCTs[16] reported a significantly higher risk of port-site hernia for the SILC technique than the other included trials. In this study, incisional adverse events (such as wound infection) were found to be the only predictor of port-site hernia. In analyses either including or excluding this particular study, the incidence of port-site hernia was found to be higher in the SILC group. Several authors[9,11,16] have claimed that a larger periumbilical incision and consequent fascial defect increase the risk of incisional hernia.

It could be argued that, depending on the shape of the patient, it can be technically difficult to fix the fascia through a small skin incision. One recent retrospective study[57] reported 500 consecutive procedures with no incisional hernia development after applying a two figure-of-eight knot instead of a one figure-of-eight knot in the SILC technique. Other authors[58] have even postulated that approaches with multiple trocar insertions through a single skin incision may have a positive effect compared with the single fascial incision.

In the present analysis, postoperative pain was similar for both techniques at all time points, apart from 12 h after surgery when patients who had SILC were found to have significantly less pain assessed by VAS than those who underwent MLC. As the difference noted was less than 1 point on a 10-point scale, the clinical importance of this finding is unclear. Many factors can affect postoperative pain, such as incision length, pneumoperitoneum pressure, use of local anaesthetics, peritoneal lavage and emotional factors. The two most recent meta-analyses showed less[11] and similar[9] postoperative pain respectively following SILC. However, findings for postoperative pain in recent RCTs differ considerably. In comparison with multiport procedures, SILC has been reported to cause less[15,17,25,35,39,44], the same[19,21,23,33,46,49] or more[16,42,47] postoperative pain at various time points. Several authors[10,59,60] have associated the higher pain score in SILC with the greater incisional trauma.

Any new technique should be at least as safe for the patient as the established technique with which it is being compared. The present study showed that complications such as intraoperative blood loss, conversion to open cholecystectomy, gallbladder perforation, intraoperative bleeding, BDI or bile leakage, haematoma, seroma and wound infection were equally common with both techniques. Furthermore, there was no difference in length of hospital stay and time to return to work.

However, BDI is considered to be the most relevant safety issue in cholecystectomy, and there have been special concerns about this with the SILC technique[61,62]. These retrospective studies showed a BDI rate of 0·7 per cent in the SILC group compared with 0·4–0·5 per cent in the MLC group. This is in contrast to the finding of a comparable BDI rate in the SILC and MLC groups in the present meta-analysis and another recent retrospective study[57]. The clinical significance of the present findings is limited by the fact that not all the included studies provided exact information on the type of biliary complications. Moreover, as the overall rate of BDI is less than 1 per cent, large numbers of patients are needed to determine the true rates[61]. It has also been stated previously that acute cholecystitis is not associated with a statistically different rate of BDI[62]; however, only three of the 37 RCTs in this meta-analysis included patients with acute cholecystitis, accounting for just 11·4 per cent of patients. It therefore remains unclear whether there will be a greater risk of BDI in the future with the (often seen) natural progression of a new technique to broader indications, such acute cholecystitis. Of interest, many surgeons perform intraoperative cholangiography (IOC) routinely with the aim of minimizing the risk of BDI. In the present study, IOC was used routinely in two RCTs[22,26]. In total, IOC was used in only 199 of 1328 interventions (15·0 per cent). This low rate could reflect a higher level of difficulty in performing IOC with a single-incision technique.

There was a trend towards a higher risk of pneumothorax after SILC, with three instances in the SILC group and none in the MLC group. The cause in one patient was the needle used to stitch the gallbladder to the peritoneum for traction[51], and the pneumothorax regressed spontaneously with conservative therapy. In a second patient, pneumothorax was caused by a laparoscopic forceps used for retracting the gallbladder, which slipped and injured the right diaphragm[19]. In the final patient, a pneumothorax apparently occurred spontaneously after operation in a patient with a history of smoking and chronic obstructive pulmonary disease. This patient required interventional chest-tube placement[15]. Pneumothorax after laparoscopic cholecystectomy is extremely rare[63]. Only two other studies reporting pneumothorax after laparoscopic cholecystectomy have been found in the literature. Kurpiewski and colleagues[64] reported two cases in a study of 100 patients undergoing SILC. Both occurred directly after putting the suspension suture into the gallbladder fundus via the seventh intercostal space. Łosin *et al.*[65] reported their first experience of three children treated with SILC. In one patient, a small pneumothorax probably resulted from placement of a relatively high stay suture. Most of these cases show that suspension sutures, which are often used in SILC, may increase the risk of pneumothorax.

The present meta-analysis has shown that there are many RCTs indicating the cosmetic superiority of SILC compared with MLC without compromising patient safety. However, this finding is not reflected in common practice where MLC remains the routine approach to benign gallbladder disease. The reasons for this are not entirely clear. The duration of surgery is significantly longer for SILC. This may be due to lack of training and/or the increased technical difficulty of SILC. Several studies[66–69] have shown that the learning curve for SILC is short, with complication rates similar to those of MLC performed by the same surgeons or rates in the literature. This refutes the argument that SILC is too difficult to perform. Surgeons need 15 min longer to perform SILC compared with MLC[9,11] which, in the authors' opinion, has limited clinical implication. Recently, it has been reported that surgeons find SILC more stressful and physically demanding to perform than MLC[70], and Lurje *et al.*[15] noted that surgeons more commonly reported discomfort while performing SILC than MLC. More significantly, the fear of higher costs[22,49] and of higher rates of port-site hernia may be preventing many clinics from introducing SILC. Another important factor could be the fact that the majority of patients receiving laparoscopic cholecystectomy are not focused on cosmesis, but on safety and freedom from symptoms.

The present meta-analysis has several limitations. First, the quality of the systematic review is partially determined by the quality of the included RCTs. Only three[15,19,21] of the 37 included trials had an overall low risk of bias. There were significant differences in the inclusion and exclusion criteria among the included trials, including whether emergency laparoscopic cholecystectomies were included. Shortcomings of the RCTs include small numbers of patients in most of the trials (20–50 per group). In addition, only six trials[15,17,19,21,44,49] were double-blinded. Another problem is the short follow-up. Only eight studies[15–17,19,21,46,47,49] reported a follow-up of 1 year or longer. Differences may have been missed owing to the high degree of heterogeneity between the studies. Two larger RCTs[71,72] have been published since the literature search for this review was completed in September 2015. Arezzo and colleagues[72] used a five-question item to evaluate the cosmetic result and did not employ any of the three scores analysed here. Guo and co-workers[71] did not evaluate the cosmetic outcome. As the cosmetic result is the primary focus of the present study, the authors consider it justifiable not to include these two recent publications. Guo *et al.*[71] stated that the primary benefit of SILC appears to be slightly less pain immediately after surgery, consistent with the present findings. Arezzo and colleagues[72] concluded that SILC is not inferior to MLC in terms of safety in selected patients undergoing cholecystectomy for benign gallbladder disease, but takes longer. An incisional hernia developed within 1 year in six patients in the SILC group and in three in the MLC group, which was not statistically significant.

In the present study, SILC provided better cosmesis and satisfaction with the wound than traditional MLC for up to a year after surgery, with comparable rates of postoperative complications, making it a safe procedure in non-obese patients in an elective setting. These advantages were achieved at cost of an increased incisional hernia rate at a follow-up ranging from 1 to 17 months after surgery. It is reasonable to consider SILC in selected patients for whom body image and cosmesis is of significant concern.

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Supporting information

Additional supporting information may be found online in the supporting information tab for this article:

Appendix S1 Characteristics of included and excluded studies (as provided by author) (Word document)

Appendix S2 Risk-of-bias assessment (Word document)

Fig. S1 Risk-of-bias assessments (Word document)

Fig. S2 Forest plot comparing intraoperative blood loss during single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S3 Forest plot comparing need for an additional trocar during single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S4 Forest plot comparing rate of conversion to open surgery during single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S5 Forest plot comparing postoperative pain at 3 h after single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S6 Forest plot comparing postoperative pain at 4 h after single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S7 Forest plot comparing postoperative pain at 8 h after single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S8 Forest plot comparing postoperative pain at 12 h after single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S9 Forest plot comparing postoperative pain at 24 h after single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S10 Forest plot comparing postoperative pain at 48 h after single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S11 Forest plot comparing postoperative pain at 72 h after single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S12 Forest plot comparing postoperative pain at 7 days after single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S13 Forest plot comparing postoperative pain at 14 days after single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S14 Forest plot comparing postoperative pain at 1 month after single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S15 Forest plot comparing length of hospital stay after single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S16 Forest plot comparing time to return to work after single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S17 Forest plot comparing rate of gallbladder perforation during single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S18 Forest plot comparing frequency of bile duct stone retention after single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S19 Forest plot comparing rate of bile leakage after single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S20 Forest plot comparing frequency of cholangiography for single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S21 Forest plot comparing rate of intraoperative bleeding during single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S22 Forest plot comparing rate of haematoma after single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S23 Forest plot comparing rate of seroma after single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S24 Forest plot comparing rate of wound infection after single-incision *versus* multiport laparoscopic cholecystectomy (Word document)

Fig. S25 Forest plot comparing rate of pneumothorax after single-incision *versus* multiport laparoscopic cholecystectomy (Word document)