REVIEW



Systematic review with meta-analysis of studies comparing single-incision laparoscopic colectomy and multiport laparoscopic colectomy

Mauro Podda¹ · Alessandra Saba¹ · Federica Porru¹ · Adolfo Pisanu¹

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Abstract

Background There is currently a paucity of research comparing the clinical outcomes of single-incision laparoscopic colectomy (SILC) with those obtained with multiport laparoscopic colectomy (MLC). This meta-analysis aimed to examine whether SILC shows real benefits over MLC, especially in terms of feasibility, safety, and oncological adequacy.

Methods A literature review of studies comparing SILC and MLC has been performed which looked at the following outcomes: mortality, morbidity, and oncological parameters of adequacy, as well as other potential benefits and drawbacks. Standardized mean difference for continuous variables and odds ratios for qualitative variables were calculated.

Results Thirty studies comparing SILC and MLC were reviewed: two prospective randomized clinical trials (RCTs), eight prospective studies, and 20 retrospective comparative observational studies. Overall, in a cohort of 3502 patients who underwent surgery, SILC was used in 1068 cases (30.5 %) and MLC was used in 2434 cases (69.5 %). Mean intraoperative blood loss was significantly lower when the SILC procedure had been used (75.06 vs. 91.45 ml, P = 0.03); bowel function recovered significantly earlier in the SILC patients (1.96 vs. 2.15 days,

P = 0.03); mean postoperative hospital stay was significantly shorter in the SILC group (5.55 vs. 6.60 days, P = 0.0005); and length of skin incision was significantly shorter in SILC patients (3.98 vs. 5.28 cm, P = 0.01). However, in the latter four outcomes, evidence of heterogeneity was found. In contrast, MLC showed significantly better results when compared to SILC in terms of distal free margins (12.26 vs. 10.98 cm, P = 0.01).

Conclusions SILC could be considered as a safe and feasible alternative to MLC in experienced hands. Further evidence for this surgical procedure should be assessed in the form of high-quality RCTs, with additional focus on its use in low rectal cancer resection.

Keywords Single-incision laparoscopic colectomy · Laparoscopy · Multiport laparoscopic colectomy · Single incision

Multiport laparoscopic colectomy (MLC) is widely accepted among surgeons as it has several advantages: a smaller incision, reduced postoperative pain, shorter hospital stay, faster return to normal activities, and improved cosmetic results when compared to the conventional open approach [1]. The oncological outcomes of MLC are also comparable with those obtained using traditional laparotomy [2].

During the 1990s, single-incision laparoscopic surgery (SILS) was used for the removal of the uterus, gallbladder, and appendix [3]. Subsequently, in 2008 two reports were published describing the preliminary use of SILS in colorectal surgery [4, 5].

The actual benefits of single-incision laparoscopic colectomy (SILC) would presumably include those of MLC, together with reduced surgical trauma, improved cosmetic results, and patient satisfaction. SILC is now used

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Mauro Podda mauropodda@ymail.com

¹ Department of Surgical Science, Chirurgia Generale, University of Cagliari, Azienda Ospedaliero-Universitaria, Presidio Policlinico di Monserrato, Blocco G, SS 554 km 4,500, 09042 Monserrato, CA, Italy

for the treatment of both benign and malignant colorectal diseases. However, the results of the SILC procedure and subsequent oncological outcomes are matters for debate. In fact, there is a paucity of research comparing the clinical outcomes of SILC with those obtained using MLC.

From 2010 onward, 30 studies comparing the clinical outcomes of SILC versus MLC have been published [6-35]. Of these studies, two were prospective, randomized trials [15, 18] and 28 were comparative prospective or retrospective observational studies [6-14, 16, 17, 19-35]. Thus far, four meta-analyses have been performed to compare the results of SILC with those obtained using MLC [36-39]. The majority of these studies were limited by a single-institution design or by small sample size. To overcome these limitations, we performed a new systematic review with meta-analysis, which included the largest number of adult patients from all comparative studies in the literature. We examined whether SILC has an advantage over MLC, in terms of feasibility, safety, and oncological adequacy. Furthermore, we aimed to verify other potential benefits and drawbacks of the technique.

Materials and methods

In this study, SILC was defined as a standardized operation performed through a single abdominal incision at the level of the umbilicus or in other abdominal regions, depending on author preference and type of colonic resection. MLC was defined as a classical laparoscopic technique, performed with three or four trocars or using a hand-assisted procedure, as similar clinical outcomes were shown in trials comparing MLC with hand-assisted technique [40, 41]. Studies comparing the characteristics and perioperative outcomes of adult patients undergoing SILC and MLC for colorectal disease met the inclusion criteria. Prospective, randomized clinical trials or prospective or retrospective observational studies comparing the two techniques were also included in the analysis. Included studies had to be written in English. Studies were excluded from the meta-analysis if the outcomes of interest (as specified below) were impossible to calculate or the standard deviation and confidence interval of the tested parameters were not reported.

A systematic literature search was performed using EMBASE, Medline, Cochrane, PubMed, and Google Scholar databases for studies comparing SILC to MLC. The following keywords: "single-incision laparoscopic colectomy" or "SILC" and "multiport laparoscopic colectomy" or "MLC" were used as search terms. The search was then extended by using the "related article" function of each database and by scanning the references of

all relevant articles. The final literature search was completed in March 2015.

The meta-analysis was performed in accordance with the recommendations from the preferred items for systematic reviews and meta-analyses statement (PRISMA) [42], and the meta-analysis of observational studies in epidemiology checklist for observational studies [43].

Two authors (MP and AP) independently extracted the following data from each study: institution and year of publication, study type, the number of patients operated on with each technique, and the baseline characteristics of patients, such as age and gender, perioperative outcomes, and postoperative results.

All included studies were reviewed for the following outcomes of interest:

- We evaluated the primary outcome measures to assess and validate safety, feasibility, and oncological efficacy of the SILC procedure. The following outcomes were reviewed: mortality and morbidity such as abdominal abscess, postoperative hematoma, wound infection, anastomotic bleeding, and anastomotic leak. Oncological outcomes reviewed: positive margins, tumor diameter, proximal and distal free margins, harvested lymph nodes, and carcinoma recurrence.
- We evaluated the secondary outcome measures to assess other potential benefits and drawbacks of SILC. The following outcomes were reviewed: previous abdominal surgery and operative outcomes such as operative time, conversion to laparotomy, intraoperative blood loss, reoperation, recovery of bowel function, readmission, length of postoperative hospital stay, length of skin incision, and incisional hernia.

The surgical indication, type of operation, and different surgical methods used for the SILC procedure were also reviewed by the authors.

Statistical analysis, synthesis, and reporting of the results

We considered variables for pooled analysis if they were previously evaluated by at least three studies. We carried out all statistical analyses using Reviewer Manager software (Review Manager—RevMan—version 5.3.5, 2014, The Nordic Cochrane Centre, Cochrane Collaboration, www.cochrane-handbook.org). The meta-analysis was conducted by searching for a numerical estimate of the outcome of interest, as described elsewhere [44]. For continuous outcomes, the Hedges' g was used for the calculation of the standardized mean difference (SMD) under the fixed-effects model, which we adjusted for small sample bias. Under the fixed-effects model, we assumed that all studies were homogeneous. We tested this assumption using the heterogeneity test, which we included to calculate the summary SMD under the random-effects model, according to the method of DerSimonian and Laird [45]. We tested for heterogeneity using the random-effects model when calculating the Chi² test and its associated P values. If this test yielded a P value <0.05, then the fixed-effects model was considered as invalid and the random-effects model as appropriate. We listed the results of the individual studies and gave the total SMD with a 95 % confidence interval (CI) for both the fixed-effects model and the random-effects model. If the value of 0 was not within the 95 % CI, then we considered the SMD statistically significant at the 5 % level (P < 0.05). The heterogeneity was also tested using the I^2 test. I^2 is the percentage of observed total variation across studies that is due to real heterogeneity, rather than chance. It is calculated as $I^2 = 100 \% \times (Q - df)/Q$, where Q is Cochran's heterogeneity statistic and df the degrees of freedom. Negative values of I^2 are considered equal to zero, so that I^2 lies between 0 % and 100 %. A value of 0 % indicates no observed heterogeneity, and larger values show increasing heterogeneity [46]. This method required the standard deviations and the confidence intervals of the tested parameters. The results of different studies were summarized and reported using a forest plot with a 95 % CI and overall SMD.

For data derived from contingency tables (qualitative outcomes), the odds ratio (OR) and 95 % CI were calculated. The ORs reported in the results are those of the pooled analysis method, also called pooled ORs. We used the Mantel-Haenszel method for calculating the weighted summary OR under the fixed-effects model and then incorporated the heterogeneity test to calculate the summary OR under the random-effects model, according to the method of DerSimonian and Laird [45]. If this test yielded a P value <0.05, then we considered the fixed-effects model as invalid and the random-effects model as appropriate. The heterogeneity was also tested using the I^2 test [46]. We have listed the results of individual studies and have given the total OR with 95 % CI for both the fixedeffects model and the random-effects model. If the value 1 was not within the 95 % CI, then we considered the OR to be statistically significant at the 5 % level (P < 0.05). We summarized the results of different studies, with 95 % CI, and the overall effect (summary OR), with 95 % CI, on a logarithmic scale using a forest plot.

Results

The PRISMA flowchart for systematic search and selection of articles for review and meta-analysis is shown in Fig. 1. We considered 30 studies comparing colorectal resections with SILC versus MLC as suitable for the pooled analysis [6-35]. Two comparative studies were excluded because there was a concern regarding duplication of data [47, 48]. The articles included in the quantitative synthesis were published between 2010 and 2015. Of these studies, ten had been conducted in the USA, four in Korea, three in Japan, two in Italy, two in Taiwan, two in the UK, two in France, one in Belgium, one in Hong Kong, one in Singapore, one in Australia, and one in the Netherlands. They included a total of 3502 patients with colon resections performed using SILC in 1068 (30.5 %) and MLC in 2434 (69.5 %) patients, respectively. In two prospective, randomized clinical trials (RCTs), the patients had been randomly assigned to either SILC or MLC groups [15, 18]. The other investigations included were eight prospective [22–25, 29–31, 35] and 20 retrospective comparative observational studies [6-14, 16, 17, 19-21, 26-28, 32-34]. The study by Katsuno et al. [16] was a poster presented at the 2012 Scientific Session of the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES).

The mean follow-up period was 15 months (range 3–35 months), as reported in the included studies [10, 15, 20, 25, 28, 29]. The two reviewers were in agreement regarding the data extracted from the studies. The characteristics of the studies, including the demographics of the included patients, indication for surgery and type of operation, and different methods used for SILC, are given in Tables 1 and 2.

The types of operation performed in the SILC group were: right hemicolectomy (586), anterior resection (171), low anterior resection (24), transverse colectomy (10), left colectomy (96), subtotal colectomy (3), sigmoidectomy (80), ileocolonic resection (46), ileocecal resection (9), total colectomy (6), proctocolectomy (17) and trans-abdominal trans-anal resection (20). The types of operation performed in the MLC group were: right hemicolectomy (799), anterior resection (583), low anterior resection (193), ileocolic resection (116), transverse colectomy (13), left colectomy (283), total colectomy (135), sigmoidectomy (55), proctectomy with TME (165), proctectomy without TME (44), Hartmann procedure (1), ileocecal resection (7), and proctocolectomy (40), as given in Table 1.

Primary outcome measures

Outcomes evaluated to assess feasibility and safety of SILC: mortality, overall morbidity, abdominal abscess, postoperative hematoma, wound infection, anastomotic bleeding, and anastomotic leak.

Mortality rate was similar in both groups, without a statistically significant difference (0.0028 vs. 0.0065, P = 0.62, OR 0.79, 95 % CI 0.31–2.01, for SILC and

Identification



Fig. 1 PRISMA flowchart for systematic search and selection of articles for review and meta-analysis

MLC, respectively; no heterogeneity was found: P = 0.98, I^2 : 0 %, Fig. 2; Table 3). One patient in the SILC group died from significant comorbidities in the postoperative period [20], a second patient died of pulmonary embolus [30], and a third patient died of neutropenic sepsis secondary to a Gram-negative urinary tract infection [33]. A total of 16 patients in the MLC group died during the postoperative period: one from a cerebrovascular accident, one from severe pneumosepsis [20], two from respiratory complications [27], two from myocardial infarction [6, 32], and ten died due to unspecified reasons [17, 23, 35].

In the meta-analysis of studies comparing overall morbidity rates after SILC (13.20 %) and MLC (13.06 %), there was no significant difference (0.132 vs. 0.130, P = 0.15, OR 0.84, 95 % CI 0.67–1.06; no heterogeneity was found: P = 0.94, I^2 : 0 %, Fig. 3; Table 3).

Abdominal abscess occurred in three patients (0.28 %) in the SILC group and in four patients (0.16 %) in the MLC group, but this difference was not significant (0.0028 vs. 0.0016, P = 0.91, OR 0.92, 95 % CI 0.24–3.52; no heterogeneity was found: P = 0.73, I^2 : 0 %, Fig. 4; Table 3).

The prevalence of postoperative hematoma was similar in both groups, being 0.37 % in the SILC group and 0.32 % in the MLC group (0.0037 vs. 0.0032, P = 0.89, OR 0.93, 95 % CI 0.34–2.55; no heterogeneity was found: P = 0.75, I^2 : 0 %, Fig. 4; Table 3).

The prevalence of wound infection was slightly higher in the SILC group (2.24 %) than in the MLC group (1.15 %), but this difference was not significant (0.0224 vs. 0.0115, P = 0.53, OR 1.18, 95 % CI 0.70–2.00; no heterogeneity was found: P = 0.98, I^2 : 0 %, Fig. 4; Table 3).

Anastomotic bleeding was shown in 1.40 % of SILC procedures and in 0.24 % of MLC procedures, but this difference was not significant (0.0140 vs. 0.0024, P = 0.10, OR 2.56, 95 % CI 0.85–7.74; no heterogeneity was found: P = 0.45, I^2 : 0 %, Fig. 5; Table 3).

The prevalence of anastomotic leak was slightly lower in the SILC group (1.87 %) than in the MLC group (4.31 %), but the difference was not significant (0.0187 vs. 0.0431, P = 0.42, OR 0.82, 95 % CI 0.51–1.33; no heterogeneity was found: P = 0.95, I^2 : 0 %, Fig. 5; Table 3). Anastomotic leak occured following anterior

Table 1 Demograph	uics char	acteristic	ur par				•						
References	Study type	No. of patients		Age (years)		Sex (M	/F)	BMI		Surgical indicatic Cancer/(on (M/B) Other	Surgical procedure	
		SILC	MLC	SILC	MLC	SILC	MLC	SILC	MLC	SILC	MLC	SILC	MLC
Chew et al. [6]	RCS	40	104	63	67	22/18	60/44	22.3	23.1	23/17	64/40	RH	RH
Kwag et al. [7]	RCS	24	48	59.5 ± 14.5	59.0 ± 13.8	9/15	18/30	24.4 ± 3	24.0 ± 2.9	24	48	AR	AR
Pedraza et al. [8]	RCS	50	50	64.6 ± 12.4	66.3 ± 12.9	25/25	23/27	27.2 ± 5.7	31.0 ± 8.1	50	50	a	р
Vasilakis et al. [9]	RCS	20	20	58.3 ± 10.7	57.9 ± 10.8	12/8	12/8	28.5 ± 4.9	29.0 ± 5.2	0/20	0/20	S	S
Yun et al. [10]	RCS	99	93	61 ± 11	59 ± 11	33/33	55/38	23.82 ± 2.81	24.23 ± 2.70	66/0	93/0	RH	RH
Currò et al. [11]	RCS	10	10	60	59	4/6	3/7	25	26	10/0	10/0	RH	RH
Egi et al. [12]	RCS	10	10	68.5	68.0	4/6	4/6	22.5	21.9	10/0	10/0	RH	RH
Fujii et al. [13]	RCS	23	23	63.9 ± 9.9	65.2 ± 9.6	10/13	13/10	21.6 ± 2.9	22.9 ± 4.5	23/0	23/0	9 RH, 11 LC, 3 AR	9 RH, 10 LC, 4 AR
Gaujoux et al. [14]	RCS	25	50	56	55	8/17	22/28	22.6	22.6	3/22	I	c	I
Huscher et al. [15]	RCT	16	16	70 ± 11	70 ± 13	6/10	<i>L/6</i>	I	I	16/0	16/0	8 RH, 8 AR	6 RH, 10 AR
Katsuno et al. [16]	RCS	100	100	64.5 ± 9.5	63.9 ± 8.7	44/56	44/56	23.4 ± 2.9	22.8 ± 2.8	100/0	100/0	50 RH, 50 LC	50 RH, 50 LC
Osborne et al. [17]	RCS	55	327	63 ± 13	1	27/28	122/ 205	26	26.6	29/26	143/184	55 AR	327 AR
Poon et al. [18]	RCT	25	25	67	67	14/11	18/7	23.2	23.6	21/4	21/4	8 RH, 2 LC, 1 S, 14 AR	9 RH, 2 LC, 1 S, 13 AR
Ramos-Valadez et al. [19]	RCS	20	20	59 ± 10	56.4 ± 12.6	11/9	11/9	25.9 ± 3.9	29.6 ± 5.4	3/17	3/17	20 S	20 S
Velthuis et al. [20]	RCS	50	50	73 ± 13.2	71 ± 11.8	21/29	22/28	25	25	41/9	40/10	50 RH	50 RH
Champagne et al. [21]	RCS	29	29	61.2 ± 4.5	63.5 ± 5.2	10/19	10/19	27.4	28.8	12/17	12/17	19 RH, 10 LC	19 RH, 10 LC
Chen et al. [22]	PCS	18	21	69.44	66.19	10/8	14/7	23.34	23.92	16/2	20/1	18 RH	21 RH
Kim et al. [23]	PCS	73	106	67	63	1	I	22.7 ± 4.0	25.6 ± 2.7	70/3	103/3	d	υ
Lai et al. [24]	PCS	14	12	72	69	4/10	4/8	24	28.5	10/4	8/4	RH	RH
Lee et al. [25]	PCS	46	46	58	61	17/29	17/29	24	25	25/21	25/21	24 RH, 18 S, 4 AR	24 RH, 18 S, 4 AR
Lu et al. [26]	RCS	27	68	60.2 ± 15.69	64.29 ± 15.06	16/11	36/32	I	I	27/0	68/0	f	60
McNally et al. [27]	RCS	27	46	67	73	13/14	21/25	27	26	20/7	39/7	ч	
Papaconstantinou et al. [28]	RCS	26	26	65 ± 13	66 土 12	11/15	11/15	28 ± 5	28 ± 5	26/0	26/0	19 RH, 4 S, 3 TrC	19 RH, 4 S, 3 TrC
Wolthuis et al. [29]	PCS	14	14	56	54	5/9	5/9	22	23	3/11	6/8	10 RH, 4 S	10 RH, 4 S
Adair et al. [30]	PCS	17	17	66.6 ± 10.0	66.7 ± 13.0	5/12	5/12	26.2 ± 4.3	25.2 ± 5.0	11/6	14/3	RH	RH
Gandhi et al. [31]	PCS	24	24	54.1 ± 8.6	56.0 ± 11.1	12/12	12/12	28.5 ± 7.2	28.5 ± 6.0	9/15	9/15	19 RH, 3 AR, 2 TC	19 RH, 3 AR, 2 TC
Waters et al. [32]	RCS	16	27	65	67	8/8	15/12	29	29	12/4	19/7	RH	RH

Table 1 continued													
References	Study type	No. of patients	10	Age (years)		Sex (M	VF)	BMI		Surgical indicatio Cancer/	on (M/B) Other	Surgical procedure	
		SILC	MLC	SILC	MLC	SILC	MLC	SILC	MLC	SILC	MLC	SILC	MLC
Keshava et al. [33]	RCS	75	74	68	74	35/40	36/38	27.0	27.3	50/25	50/24	RH	RH
Lim et al. [34]	RCS	4	263	63.9 ± 9.9	63.8 ± 11.1	28/16	170/93	23.7 ± 3.1	23.8 ± 3.2	44/0	263/0	11 RH, 15 AR, 18 LAR	52 RH, 82 AR, 129 LAR
Khayat et al. [35]	PCS	84	715	46 ± 18	53 土 17	25/59	377/ 338	22 ± 3.6	24 土 4.6	15/69	319/396	í	×
Total or mean		1068	2434	63.02	63.62			24.86	25.67	769/ 299	1602/ 781		
<i>BMI</i> body mass indeprospective compara colectomy, <i>TC</i> total	ex, <i>SILC</i> tive stud colecton	7 single-i ly, <i>M/B</i> n ny, <i>STC</i>	incision naligna subtota	n laparoscopic (nt/benign disea nl colectomy	colectomy, <i>MLC</i> se, <i>RH</i> right herr	7 multipc iicolecto.	ort laparc my, AR a	sscopic colecto interior resectic	my, RCS retros on, S sigmoidec	spective c tomy, <i>LC</i>	omparative left colecto	study, <i>RCT</i> randomiz my, <i>LAR</i> low anterior 1	ed controlled trial, PCS esection, TrC transverse
^{a,b} 33 RH, 2 TrC, 2	LC, 12	AR, 1 S	TC										
^c 8 RH, 7 S, 4 ileoc	secal rese	ection, 3	protect	tomy, 2 STC, 1	l redo ileocoloni	c resecti	on						
^d 20 RH, 1 TC, 4 L	C, 16 A	R, 6 LAI	R, 8 pr	octocolectomy,	18 transabdomi	nal and	transanal	resection					
^e 28 RH, 1 TC, 10 /	AR, 54 I	LAR, 1 5	S, 2 TC	C, 1 Hartmann,	8 proctocolector	ny, 1 LC	()						
^f 17 AR, 8 RH, 1 L ⁱ	C, 1 TC												
^g 40 AR, 16 RH, 3	LC, 5 T ⁱ	C, 4 ST(()										
^h 5 Ileocecectomy, 9	9 RH, 5	TrC, 2 I	., C, 6 S										
ⁱ 7 Ileocecectomy, 2	28 RH, 3	TrC, 1	LC, 7 {	S									
^j 43 Ileocolic resecti	ion, 15 l	RH, 14 L	.C, 2 pi	roctectomy with	h TME, 3 procté	sctomy v	vithout T	TME, 4 TC/ST	C, 3 total colop	roctecton	Ŋ		
k 116 Ileocolic resec	ction, 84	RH, 20	4 LC, 1	165 proctectom	y with TME, 44	proctec	tomy wit	thout TME, 70	TC/STC, 32 tc	otal colopi	roctectomy		

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Table 2 Methods for single-incision laparoscopic colectomy as reported in the included studies

References	Device
Chew et al. [6]	SILS Ports (Covidien, Norwalk, CT, USA); SSL Access system (Ethicon Endo-Surgery Cincinnati, OH, USA); TriPort system (Advanced Surgical Concepts, Wicklow, Ireland)
Kwag et al. [7]	ALEXIS Wound Retractor (Applied Medical, Rancho Santa Margarita, CA, USA); SILS Ports (Covidien Norwalk, CT, USA)
Pedraza et al. [8]	SILS Port Multiple Instrument Access Port (Covidien, Mansfield, MA, USA); GelPOINT Advanced Access Platform (Applied Medical, Rancho Santa Margarita, CA, USA).
Vasilakis et al. [9]	SILS Port (Covidien: Mansfield, MA, USA)
Yun et al. [10]	Latex glove, Skin Angle (TERANG NUSA SDN BHD, Kota Bharu, Kelantan, Malaysia), 3–4 Separator access system (Appl. Medical, Rancho Santa Margarita, CA, USA), Alexis O wound retractor (Appl. Medical).
Currò et al. [11]	SILS TM Port (Covidien, Norwalk, CT, USA); Endocone system (Karl Storz GmbH & Co. KG, Tuttlingen, Germany)
Egi et al. [12]	GelPort (Applied Medical, Rancho Santa Margarita, CA, USA)
Fujii et al. [13]	The SILS TM Port (Covidien, Mansfield, MA, USA); SILSTM Port 5 and Port 12 (which adds a trocar 12 mm in diameter).
Gaujoux et al. [14]	SILS TM Port Multiple Instrument Access Port, Covidien, Inc., Norwalk, CT or GelPOINT TM advanced access platform, Applied Medical, Rancho Santa Margarita, CA, USA)
Huscher et al. [15]	SILS device (Covidien)
Katzuno et al. [16]	SILS Port
Osborne et al. [17]	Olympus TriPort (Olympus, Southend, UK)
Poon et al. [18]	Triport access system (Olympus), OCTO TM Single-Port System
Ramos-Valadez et al. [19]	SILS TM Port (Covidien, Mansfield, MA, USA); GelPOINTTM (Applied Medical, Rancho Santa Margarita, CA, USA); GelPort (Applied Medical).
Velthuis et al. [20]	Covidien (Covidien, Mansfield, Mass., USA); TriPort by Olympus (Olympus, Hamburg, Germany)
Champagne et al. [21]	SILS Port (Covidien, Norwalk, CT, USA)
Chen et al. [22]	_
Kim et al. [23]	Homemade single port, wound retractor (ALEXIS wound retractor XS), surgical glove; OCTO Port (Dalim, Korea); SILS port (single-incision laparoscopic surgery port, Covidien)
Lai et al. [24]	Olympus Quadport (Olympus Medical System Corp., Tokyo, Japan)
Lee et al. [25]	Quadport access system (Olympus America, Center Valley, PA, USA); GelPOINT access platform (Applied Medical, Rancho Santa Margarita, CA, USA); Spider surgical system (TransEnterix, Durham, NC, USA); SILS Port (Covidien, Mansfield, MA, USA)
Lu et al. [26]	Home-made multiple-port system
McNally et al. [27]	SILS Port (Covidien, Norwalk, CT, USA); GelPort (Applied Medical); SSL Port (Ethicon, Cincinnati, OH, USA)
Papaconstantinou et al. [28]	SILS Port (Covidien, Mansfield, MA, USA)
Wolthuis et al. [29]	SILS Port (Covidien, Mansfield, Massachusetts, USA); Quadport (Olympus, Medical Europe Holding GmbH, Hamburg, Germany); GelPOINT (Applied Medical, Rancho, Santa Margarita, California, USA); single-site laparoscopic access system (Ethicon Endo-surgery Inc., Cincinnati, Ohio, USA)
Adair et al. [30]	GelPort (Applied Medical, Rancho Santa Margarita, CA, USA); GelPOINT (Applied Medical, Rancho Santa Margarita, CA, USA); SILS Port (Covidien, Norwalk, CN, USA); TriPort (Advanced Surgical Concepts, Wicklow, Ireland)
Gandhi et al. [31]	SILS Port Multiple Instrument Access Port (Covidien, Mansfield, MA, USA); GelPOINT (Applied Medical, Rancho Santa Margarita, CA, USA); GelPort (Applied Medical)
Waters et al. [32]	SILS Port Covidien Inc. (Mansfield, MA, USA)
Keshava et al. [33]	GelPort device (Applied Medical, Rancho Santa Margarita, California, USA); GelPOINT (Applied Medical)
Lim et al. [34]	OCTO single-port system (OT304, Dalim Co.)
Khayat et al. [35]	-

resection in both groups. However, the number of low anterior resections in SILC colectomies was just 24 out of 195 (12.3 %) compared with 193 out of 776 (24.9 %) in the MLC group. This difference was statistically significant

 $(P = 0.01, \text{ by } \chi^2 \text{ test})$. Moreover, the number of right colectomies performed in the SILC group was significantly higher than the MLC group (0.56 vs. 0.41, P = 0.000, by χ^2 test).

	SIL	2	MLC	2		Odds Ratio			Odds	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	Year		M-H, Fixe	d, 95% CI	
Waters et al. 2010	0	16	1	27	10.7%	0.54 [0.02, 13.93]	2010				
Adair et al. 2010	1	17	0	17	4.5%	3.18 [0.12, 83.76]	2010				
McNally et al. 2011	0	27	2	46	17.8%	0.32 [0.01, 7.00]	2011				
Kim et al. 2011	0	73	1	106	11.9%	0.48 [0.02, 11.91]	2011	-	•		
Velthuis et al. 2012	1	50	2	50	19.1%	0.49 [0.04, 5.58]	2012		· · · · ·		
Osborne et al. 2012	0	55	3	327	9.8%	0.84 [0.04, 16.39]	2012				
Keshava et al. 2013	1	75	0	74	4.8%	3.00 [0.12, 74.84]	2013			•	
Chew et al. 2013	0	40	1	104	8.1%	0.85 [0.03, 21.34]	2013	-			
Khayat et al. 2015	0	84	6	715	13.3%	0.65 [0.04, 11.57]	2015	-	•		
Total (95% CI)		437		1466	100.0%	0.79 [0.31, 2.01]					
Total events	3		16								
Heterogeneity: Chi ² =	2.00, df	= 8 (P	= 0.98);	$l^2 = 0\%$				0.01	01	10	100
Test for overall effect:	Z = 0.50	(P = 0	.62)					0.01	Favours [SILC]	Favours [MLC]	100

Fig. 2 Meta-analysis of mortality rate

 Table 3 Postoperative outcomes 1

References	Mortality		Morbidity		Abdomina	l abscess	Postoperativ	ve hematoma
	SILC	MLC	SILC	MLC	SILC	MLC	SILC	MLC
Chew et al. [6]	0	1	9	22	_	_	_	_
Kwag et al. [7]	0	0	2	4 ^a	-	-	_	-
Pedraza et al. [8]	0	0	4	7	-	-	_	-
Vasilakis et al. [9]	0	0	1	3	0	1	_	-
Yun et al. [10]	0	0	6	14	-	-	1	2
Currò et al. [11]	0	0	2	1	0	0	_	_
Egi et al. [12]	0	0	0	0	0	0	0	0
Fujii et al. [13]	0	0	3	5	-	-	_	-
Gaujoux et al. [14]	0	0	1	8	-	-	_	-
Huscher et al. [15]	0	0	3	5	-	-	_	-
Katsuno et al. [16]	0	0	5	6	-	-	_	-
Osborne et al. [17]	0	3	4	13	_	_	1	2
Poon et al. [18]	0	0	1	3	_	_	_	_
Ramos-Valadez et al. [19]	0	0	2	2	_	_	1	0
Velthuis et al. [20]	1	2	17	17	2	1	0	2
Champagne et al. [21]	-	-	5	7	-	-	_	-
Chen et al. [22]	0	0	3	2	0	1	_	-
Kim et al. [23]	0	1	23	39	-	-	_	-
Lai et al. [24]	0	0	0	0	0	0	0	0
Lee et al. [25]	0	0	0	0	0	0	0	0
Lu et al. [26]	0	0	14	29	0	0	0	1
McNally et al. [27]	0	2	5	16	0	0	0	0
Papaconstantinou et al. [28]	0	0	_	-	-	-	_	-
Wolthuis et al. [29]	0	0	0	0	0	0	0	0
Adair et al. [30]	1	0	5	4	0	0	0	1
Gandhi et al. [31]	0	0	2	0	0	0	0	0
Waters et al. [32]	0	1	3	4	1	1	0	0
Keshava et al. [33]	1	0	8	13	0	0	1	0
Lim et al. [34]	0	0	7	46	-	-	_	-
Khayat et al. [35]	0	6	6	48	-	_	-	-
Total or mean	3	16	141	318	3	4	4	8
	(0.28 %)	(0.65 %)	(13.20 %)	(13.06 %)	(0.28 %)	(0.16 %)	(0.37 %)	(0.32 %)

Table 3 continued

References	Wound in	fection	Anastomoti	ic bleeding	Anastomot	ic leak	Hospital sta	y (days)
	SILC	MLC	SILC	MLC	SILC	MLC	SILC	MLC
Chew et al. [6]	3	6	0	1	0	3	5	5
Kwag et al. [7]	_	-	-	-	2	1	7.1 ± 3.4	8.1 ± 3.5
Pedraza et al. [8]	-	-	-	-	-	-	4.5 ± 3.7	4 ± 1.7
Vasilakis et al. [9]	1	2	-	-	0	1	3.9 ± 1.6	5.5 ± 2.0
Yun et al. [10]	3	1	-	-	0	0	8 ± 4	9 ± 5
Currò et al. [11]	1	0	-	-	1	0	6	6
Egi et al. [12]	0	0	0	0	0	0	8.0	10.5
Fujii et al. [13]	1	3	0	0	0	0	8.2 ± 3.4	12.7 ± 12.9
Gaujoux et al. [14]	-	-	-	-	0	3	6	7
Huscher et al. [15]	1	2	-	-	0	1	6 ± 3	7 ± 2
Katsuno et al. [16]	2	2	-	-	1	-	9.6 ± 1.8	9.7 ± 2.6
Osborne et al. [17]	-	-	2	0	1	11	1	3
Poon et al. [18]	1	2	-	-	-	-	4	5
Ramos-Valadez et al. [19]	1	0	0	0	0	0	3.2 ± 1.0	3.8 ± 2.1
Velthuis et al. [20]	4	3	-	-	1	3	6	6
Champagne et al. [21]	-	-	-	-	-	-	3.7	3.9
Chen et al. [22]	1	0	-	-	0	0	5	5
Kim et al. [23]	1	2	-	-	6	7	9.6 ± 9.6	15.5 ± 9.8
Lai et al. [24]	0	0	0	0	0	0	3.5	4
Lee et al. [25]	0	0	0	0	0	0	4.6 ± 1.6	4.3 ± 0.8
Lu et al. [26]	1	0	0	0	0	0	7	7
McNally et al. [27]	0	1	0	0	0	1	3	5
Papaconstantinou et al. [28]	-	-	-	-	-	-	3.6 ± 1.6	5.0 ± 2.2
Wolthuis et al. [29]	0	0	0	0	0	0	7	6
Adair et al. [30]	1	1	0	0	0	1	3.9 ± 3.7	4.1 ± 2.2
Gandhi et al. [31]	1	0	1	0	0	0	2.7 ± 0.8	3.3 ± 1.1
Waters et al. [32]	1	1	0	0	0	1	5	6
Keshava et al. [33]	0	1	1	1	0	0	5	8
Lim et al. [34]	0	1	1	4	2	12	8.2 ± 2.3	8.8 ± 4.6
Khayat et al. [35]	-	-	-	-	6	60	8 ± 6	10 ± 7
Total or mean	24	28	5	6	20	105	5.55	6.60
	(2.24 %)	(1.15 %)	(1.40 %)	(0.24 %)	(1.87 %)	(4.31 %)		

SILC single-incision laparoscopic colectomy, MLC multiport laparoscopic colectomy

^a 3 chilous ascitis

Outcomes evaluated to assess oncological efficacy of SILC: positive margins, proximal and distal free margins, harvested lymph nodes, and carcinoma recurrence.

It was impossible to meta-analyze the outcome regarding positive margins after colonic resection because all authors reported negative margins. There was no statistically significant difference between SILC and MLC groups regarding tumor diameter (3.43 vs. 3.56 cm, P = 0.85, SMD = 0.01, 95 % CI -0.13 to 0.16; no heterogeneity was found: P = 0.067, I^2 : 46 %, Table 4). Average proximal free margin from the tumor was similar in both the SILC group and the MLC group (13.01 vs. 11.35 cm, P = 0.53, SMD = 0.09, 95 % CI -0.19 to 0.37; heterogeneity was

found: P = 0.01, I^2 : 66 %, Fig. 6; Table 4). However, average distal free margin from the tumor was significantly longer in the MLC group than in the SILC group (12.26 vs. 10.98 cm, P = 0.01, SMD = 0.19, 95 % CI 0.04–0.35; no heterogeneity was found: P = 0.14, I^2 : 38 %, Fig. 6; Table 4). The number of harvested lymph nodes was similar in the SILC group and in the MLC group (18.59 vs. 18.82 lymph nodes, P = 0.23, SMD = 0.11, 95 % CI –0.07 to 0.28; heterogeneity was found: P = 0.01, I^2 : 53 %, Fig. 6; Table 4). Only three studies reported results regarding tumor recurrence, with a mean follow-up of 15 months. The lack of further follow-up data made comprehensive meta-analysis of this outcome impossible.

	SIL	C	MLO	C		Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	Year	M-H, Fixed, 95% CI
Waters et al. 2010	3	16	4	27	1.6%	1.33 [0.26, 6.87]	2010	
Adair et al. 2010	5	17	4	17	1.8%	1.35 [0.29, 6.26]	2010	
Gandhi et al. 2010	2	24	0	24	0.3%	5.44 [0.25, 119.63]	2010	
Champagne et al. 2011	5	29	7	29	3.7%	0.65 [0.18, 2.37]	2011	
Kim et al. 2011	23	73	39	106	14.0%	0.79 [0.42, 1.49]	2011	
Chen et al. 2011	3	18	2	21	1.0%	1.90 [0.28, 12.87]	2011	
Lu et al. 2011	14	27	29	68	5.1%	1.45 [0.59, 3.54]	2011	_ +•
McNally et al. 2011	5	27	16	46	6.2%	0.43 [0.14, 1.34]	2011	
Fujii et al. 2012	3	23	5	23	2.8%	0.54 [0.11, 2.59]	2012	
Currò et al. 2012	2	10	1	10	0.5%	2.25 [0.17, 29.77]	2012	
Huscher et al. 2012	3	16	5	16	2.6%	0.51 [0.10, 2.62]	2012	
Gaujoux et al. 2012	1	25	8	50	3.3%	0.22 [0.03, 1.86]	2012	
Velthuis et al. 2012	17	50	17	50	7.2%	1.00 [0.44, 2.29]	2012	
Osborne et al. 2012	4	55	13	327	2.2%	1.89 [0.59, 6.04]	2012	
Katsuno et al. 2012	5	100	6	100	3.7%	0.82 [0.24, 2.79]	2012	
Ramos-Valadez et al. 2012	2	20	2	20	1.2%	1.00 [0.13, 7.89]	2012	
Poon et al. 2012	1	25	3	25	1.8%	0.31 [0.03, 3.16]	2012	
Chew et al. 2013	9	40	22	104	6.1%	1.08 [0.45, 2.61]	2013	
Pedraza et al. 2013	4	50	7	50	4.1%	0.53 [0.15, 1.95]	2013	
Kwag et al. 2013	2	24	4	48	1.6%	1.00 [0.17, 5.89]	2013	
Yun et al. 2013	6	66	14	93	6.8%	0.56 [0.20, 1.55]	2013	
Vasilakis et al. 2013	1	20	3	20	1.8%	0.30 [0.03, 3.15]	2013	
Keshava et al. 2013	8	75	13	74	7.5%	0.56 [0.22, 1.44]	2013	
Lim et al. 2014	7	44	46	263	7.1%	0.89 [0.37, 2.13]	2014	
Khayat et al. 2015	6	84	48	715	6.0%	1.07 [0.44, 2.58]	2015	
Total (95% CI)		958		2326	100.0%	0.84 [0.67, 1.06]		•
Total events	141		318					
Heterogeneity: Chi ² = 14.45,	df = 24 (P = 0.9	(4); $I^2 = 1$	0%				
Test for overall effect: $Z = 1.4$	5 (P = 0)	.15)						Favours [SILC] Favours [MLC]
								ravours [siee] Tavours [wee]

Fig. 3 Meta-analysis of overall morbidity

Secondary outcome measures

Outcomes evaluated to assess other potential benefits and drawbacks of SILC: body mass index (BMI), previous abdominal surgery, operative time, conversion to laparotomy, intraoperative blood loss, reoperation, recovery of bowel functions, readmission, length of postoperative hospital stay, and length of skin incision.

The BMI was significantly lower in the SILC group compared with the MLC group (24.86 vs. 25.67 kg/m², P = 0.04, SMD = -0.22, 95 % CI -0.43 to -0.001; heterogeneity was found: P < 0.0001, l^2 : 71 %, Table 1).

Previous abdominal surgery was not a contraindication when performing both SILC and MLC procedures. A previous abdominal operation was performed in 14.23 % of patients in the SILC group versus 14.50 % of patients in the MLC group. This difference was not significant (P = 0.12, OR 0.82, 95 % CI 0.65–1.05; no heterogeneity was found: P = 0.93, I^2 : 0 %, Table 5). A history of previous abdominal operations was not always reported in the included studies.

No statistically significant difference was found in the meta-analysis of studies comparing SILC and MLC for operative time (147.28 vs. 148.97 min, P = 0.58, SMD = 0.09, 95 % CI -0.22 to 0.39; heterogeneity was found: P < 0.00001, l^2 : 85 %, Fig. 7; Table 5).

The rate of conversion to laparotomy was lower in the SILC group (1.40 %) than in the MLC group (3.12 %), but this difference was not significant (0.0140 vs. 0.0312, P = 0.11, OR 0.64, 95 % CI 0.38–1.10; no heterogeneity was found: $P = 0.91, I^2: 0 \%$, Fig. 8; Table 5). The reasons for conversion to open surgery in the SILC group were: two large tumors, two dense adhesions, one bulky omentum, one case of dense retroperitoneal fibrosis, one case of inability to identify left ureter, one case of ileocolic artery bleeding, one mesenteric tearing, one difficult splenic flexure mobilization, two cases of severe inflammation, and one case of intraoperative colonic injury. The reasons for conversion to open surgery in the MLC group were: six adhesions, one case of inability to visualize the tattoo, one case of poor visibility for thick omentum, one dilated proximal bowel, one large tumor, one diverticular abscess, one case of anatomical difficulties, one bleeding of the inferior mesenteric artery, one case of inability to laparoscopically separate the left ureter from an abscess, one case of intraoperative vascular complications, and 61 unspecified cases. According to the most part of authors, we considered conversion from SILC to MLC, even if only one additional trocar was used. The reasons for conversion from SILC to MLC were: three cases of difficult exposure of the peritoneal reflection, 14 cases of difficult pelvic wall dissection, six adhesions, one case of bleeding of the gonadic artery, one discovery of a bulky

A											
	SILC	2	MLC	2		Odds Ratio			Odds	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	Year		M-H, Fixe	d, 95% CI	
Waters et al. 2010	1	16	1	27	15.6%	1.73 [0.10, 29.78]	2010				- 1
Chen et al. 2011	0	18	1	21	30.2%	0.37 [0.01, 9.64]	2011				
Velthuis et al. 2012	2	50	1	50	21.4%	2.04 [0.18, 23.27]	2012			-	
Vasilakis et al. 2013	0	20	1	20	32.7%	0.32 [0.01, 8.26]	2013	-			
Total (95% CI)		104		118	100.0%	0.92 [0.24, 3.52]					
Total events	3		4								
Heterogeneity: $Chi^2 = 1$	L.31, df =	= 3 (P =	= 0.73);	$ ^2 = 0\%$				0.01		10	100
Test for overall effect: 2	Z = 0.12	(P = 0)	.91)					0.01	Favours [SILC]	Favours [MLC]	100
В											

	SILC	-	MLC	2		Odds Ratio			Odds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	Year		M-H, Fixed, 95% CI	
Adair et al. 2010	0	17	1	17	18.4%	0.31 [0.01, 8.27]	2010			
Lu et al. 2011	0	27	1	68	10.7%	0.82 [0.03, 20.71]	2011	-		
Ramos-Valadez et al. 2012	1	20	0	20	5.8%	3.15 [0.12, 82.16]	2012			
Velthuis et al. 2012	0	50	2	50	31.2%	0.19 [0.01, 4.10]	2012	•		
Osborne et al. 2012	1	55	2	327	7.1%	3.01 [0.27, 33.76]	2012			
Yun et al. 2013	1	66	2	93	20.6%	0.70 [0.06, 7.88]	2013			
Keshava et al. 2013	1	75	0	74	6.2%	3.00 [0.12, 74.84]	2013			
Total (95% CI)		310		649	100.0%	0.93 [0.34, 2.55]			-	
Total events	4		8							
Heterogeneity: Chi ² = 3.45, d	f = 6 (P =	= 0.75)	; $ ^2 = 0\%$					0.01	0 1 1 10	100
Test for overall effect: $Z = 0.1$	3 (P = 0.)	89)						0.01	Favours [SILC] Favours [MLC]	100

С											
	SIL	C	MLG	C		Odds Ratio			Odds Rat	io	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	Year		M-H, Fixed, S	95% CI	
Adair et al. 2010	1	17	1	17	3.7%	1.00 [0.06, 17.41]	2010			<u> </u>	
Gandhi et al. 2010	1	24	0	24	1.8%	3.13 [0.12, 80.68]	2010				
Waters et al. 2010	1	16	1	27	2.7%	1.73 [0.10, 29.78]	2010				-1
McNally et al. 2011	0	27	1	46	4.3%	0.55 [0.02, 14.02]	2011				
Kim et al. 2011	1	73	2	106	6.3%	0.72 [0.06, 8.12]	2011				
Lu et al. 2011	1	27	0	68	1.1%	7.75 [0.31, 196.40]	2011				\rightarrow
Chen et al. 2011	1	18	0	21	1.7%	3.69 [0.14, 96.22]	2011				
Katsuno et al. 2012	2	100	2	100	7.7%	1.00 [0.14, 7.24]	2012				
Huscher et al. 2012	1	16	2	16	7.4%	0.47 [0.04, 5.73]	2012		· · · · · ·		
Fujii et al. 2012	1	23	3	23	11.3%	0.30 [0.03, 3.15]	2012	-			
Velthuis et al. 2012	4	50	3	50	10.8%	1.36 [0.29, 6.43]	2012				
Ramos-Valadez et al. 2012	1	20	0	20	1.8%	3.15 [0.12, 82.16]	2012			-	
Poon et al. 2012	1	25	2	25	7.5%	0.48 [0.04, 5.65]	2012				
Currò et al. 2012	1	10	0	10	1.7%	3.32 [0.12, 91.60]	2012			÷	
Keshava et al. 2013	0	75	1	74	5.9%	0.32 [0.01, 8.09]	2013		•		
Yun et al. 2013	3	66	1	93	3.1%	4.38 [0.45, 43.08]	2013				_
Vasilakis et al. 2013	1	20	2	20	7.4%	0.47 [0.04, 5.69]	2013		· · · · · ·		
Chew et al. 2013	3	40	6	104	12.1%	1.32 [0.31, 5.57]	2013				
Lim et al. 2014	0	44	1	263	1.7%	1.97 [0.08, 49.03]	2014				-
Total (95% CI)		691		1107	100.0%	1.18 [0.70, 2.00]			+		
Total events	24		28								
Heterogeneity: $Chi^2 = 8.21$, d	f = 18 (P)	= 0.98	3); $I^2 = 0$	%							
Test for overall effect: $Z = 0.6$	53 (P = 0)	.53)						0.01	0.1 1	10	100
									Favours [SILC] Fav	ours [MLC]	

Fig. 4 Meta-analyses of specific complications. A Abdominal abscess; B postoperative hematoma; C wound infection

tumor with presacral fixation, one dense pelvic abscess cavity, one redundant sigmoid colon, one case of inadequate colonic traction, one friable Crohn's mesentery, one unclear anatomy, and 34 unspecified cases.

Mean intraoperative blood loss was significantly lower in the SILC group than in the MLC group (75.06 vs. 91.45 ml, P = 0.03, SMD = -0.26, 95 % CI -0.48 to -0.03; heterogeneity was found: P = 0.03, I^2 : 53 %, Fig. 7; Table 5).

The reoperation rate was slightly lower in the SILC group (1.38 %) than in the MLC group (2.75 %), but not significantly (0.0138 vs. 0.0275, P = 0.50, OR 0.79, 95 %

CI 0.40–1.56; no heterogeneity was found: P = 0.78, I^2 : 0 %, Fig. 9; Table 5). The reasons for reoperation were: anastomotic leak, postoperative bleeding, intraabdominal abscess, fascial dehiscence, perforation for cecal ischemia, and thermal injury of the transverse colon.

Bowel function recovered significantly earlier in terms of flatus in the SILC group compared with the MLC group (1.96 vs. 2.15 days, P = 0.03, SMD = -0.28, 95 % CI -0.53 to -0.03; heterogeneity was found: P = 0.04, I^2 : 59 %, Fig. 10; Table 6). We did not meta-analyze data regarding starting a postoperative regular diet because only two studies reported mean and standard deviation [7, 23].

Α

	SILC	C	MLG	2		Odds Ratio			Odds Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	Year		M-H, Fixed, 95% Cl	í –	
Gandhi et al. 2010	1	24	0	24	13.2%	3.13 [0.12, 80.68]	2010				_
Osborne et al. 2012	2	55	0	327	3.9%	30.61 [1.45, 646.34]	2012				\rightarrow
Chew et al. 2013	0	40	1	104	23.4%	0.85 [0.03, 21.34]	2013	-			
Keshava et al. 2013	1	75	1	74	27.9%	0.99 [0.06, 16.07]	2013				
Lim et al. 2014	1	44	4	263	31.5%	1.51 [0.16, 13.79]	2014				
Total (95% CI)		238		792	100.0%	2.56 [0.85, 7.74]			-		
Total events	5		6								
Heterogeneity: Chi ² =	3.67, df :	= 4 (P =	= 0.45);	$ ^2 = 0\%$				0.01	01 1	10	100
Test for overall effect:	Z = 1.67	(P = 0	.10)					0.01	Favours [SILC] Favours [[MLC]	100

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	SIL	C	MLG	C		Odds Ratio		Odds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	Year	M-H, Fixed, 95%	CI
Adair et al. 2010	0	17	1	17	3.8%	0.31 [0.01, 8.27]	2010		
Waters et al. 2010	0	16	1	27	2.8%	0.54 [0.02, 13.93]	2010		
McNally et al. 2011	0	27	1	46	2.8%	0.55 [0.02, 14.02]	2011		
Kim et al. 2011	6	73	7	106	13.6%	1.27 [0.41, 3.94]	2011		
Currò et al. 2012	1	10	0	10	1.1%	3.32 [0.12, 91.60]	2012		
Velthuis et al. 2012	1	50	3	50	7.6%	0.32 [0.03, 3.18]	2012		
Katsuno et al. 2012	1	100	0	100	1.3%	3.03 [0.12, 75.28]	2012		
Osborne et al. 2012	1	55	11	327	8.0%	0.53 [0.07, 4.20]	2012		
Gaujoux et al. 2012	0	25	3	50	6.0%	0.27 [0.01, 5.36]	2012	· · · · · · · · · · · · · · · · · · ·	-
Huscher et al. 2012	0	16	1	16	3.8%	0.31 [0.01, 8.28]	2012		
Vasilakis et al. 2013	0	20	1	20	3.8%	0.32 [0.01, 8.26]	2013		
Kwag et al. 2013	2	24	1	48	1.6%	4.27 [0.37, 49.68]	2013		
Chew et al. 2013	0	40	3	104	5.0%	0.36 [0.02, 7.09]	2013		_
Lim et al. 2014	2	44	12	263	8.5%	1.00 [0.22, 4.61]	2014		<u>.</u>
Khayat et al. 2015	6	84	60	715	30.3%	0.84 [0.35, 2.01]	2015		
Total (95% CI)		601		1899	100.0%	0.82 [0.51, 1.33]		•	
Total events	20		105						
Heterogeneity: $Chi^2 = 1$	644 df	= 14 (P	= 0.95	$1^2 = 0^4$	%				_
Test for overall effect	7 = 0.81	(P = 0)	47)	, 0.				0.01 0.1 1	10 100
resctor overan enece.	- 0.01							Favours [SILC] Favour	s [MLC]

Fig. 5 Meta-analyses of specific complications. A Anastomotic bleeding; B anastomotic leak

The rate of readmission was moderately lower in the SILC group (0.93 %) than in the MLC group (1.23 %), but not significantly (0.0093 vs. 0.0123, P = 0.83, OR 0.92, 95 % CI 0.44–1.93; no heterogeneity was found: P = 0.49, I^2 : 0 %, Table 6). The reasons for readmission were ileus, anastomotic leak, abdominal hematoma, abdominal abscess, wound infection, and stroke-like symptoms.

Mean postoperative hospital stay was significantly shorter in the SILC group than in the MLC group (5.55 vs. 6.60 days, P = 0.0005, SMD = -0.27, 95 % CI -0.42 to -0.12; heterogeneity was found: P = 0.02, I^2 : 47 %, Fig. 7; Table 3).

Length of skin incision was significantly shorter in the SILC group than in the MLC group (3.98 vs. 5.28 cm, P = 0.01, SMD = -0.94, 95 % CI -1.65 to -0.22; heterogeneity was found: P < 0.00001, I^2 : 93 %, Fig. 10; Table 5).

Subgroup analysis: right hemicolectomies

Complications were reported for 16.7 % of patients who underwent a right hemicolectomy in the SILC group and for 15.3 % of patients in the MLC group, without any statistically significant difference (OR 1.06, 95 % CI 0.70–1.59, P = 0.79; no heterogeneity was found for $I^2 = 0$ %; P = 0.82). No significant difference was reported for operative time (SMD, -0.19, 95 % CI -0.48 to 0.10, P = 0.20; no heterogeneity was found for $I^2 = 20$ %; P = 0.26), and postoperative hospital stay (SMD, -0.19, 95 % CI -0.47 to 0.10, P = 0.20; no heterogeneity was found for $I^2 = 0$ %; P = 0.26).

Subgroup analysis: anterior resections

Complications were reported for 7.6 % of patients who underwent an anterior resection in the SILC group and for 4.5 % of patients in the MLC group, without any significant difference (OR 1.52, 95 % CI 0.57–4.05, P = 0.40; no heterogeneity was found for $I^2 = 0$ %; P = 0.55). No significant difference was reported for operative time (SMD, -0.27, 95 % CI -1.32 to 0.77, P = 0.61; heterogeneity was found for $I^2 = 93$ %; P = 0.0003) and conversion to laparotomy, the rate being 1.3 % in the SILC

Table 4 Oncological outcomes

References	Pos ma	sitive margins rgins	Specimen len (cm)	gth (cm)	Tu: (cn	mor diame n)	ter (cm)	Proximal free free margin (e margin (cm) cm)
	SII	LC MLC	SILC	MLC	SII	LC	MLC	SILC	MLC
Chew et al. [6]	_	_	19	20	2.5		3.0	8.5	9.5
Kwag et al. [7]	0	0	20.1 ± 3.8	21.3 ± 4.1	6 2.6	± 1.3	3.4 ± 1.9	11.2 ± 3.9	11.4 ± 4.1
Pedraza et al. [8]	0	0	_	-	_		_	-	-
Vasilakis et al. [9]	_	_	_	_	_		_	_	_
Yun et al. [10]	0	0	_	-	4.0	± 2.7	4.1 ± 2.4	14.4 ± 8.4	15.0 ± 7.8
Currò et al. [11]	_	_	_	-	2.6		2.7	-	-
Egi et al. [12]	_	_	_	-	_		_	-	-
Fujii et al. [13]	0	0	_	-	2.3	5 ± 1.15	2.72 ± 1.34	8.8 ± 2.4	8.5 ± 3.9
Gaujoux et al. [14]	_	_	_	-	_		_	-	-
Huscher et al. [15]	0	0	24 ± 9	24 ± 10	_		_	-	-
Katsuno et al. [16]	_	_	_	-	_		_	-	-
Osborne et al. [17]	_	_	_	_	_		_	_	_
Poon et al. [18]	_	_	_	_	3.5		4.0	8.0	8.0
Ramos-Valadez et al. [19]	0	0	_	_	_		_	_	_
Velthuis et al. [20]	0	0	26.13 ± 6.9	25.89 ± 8	.9 4.8	1 ± 1.6	4.64 ± 1.8	_	_
Champagne et al. [21]	0	0	43.5	44.2	_		_	_	_
Chen et al. [22]	0	0	_	_	2		2.5	_	_
Kim et al. [23]	0	0	_	_	5.5	± 2.6	4.6 ± 2.3	33.4 ± 30.3	17.9 ± 20.5
Lai et al. [24]	0	0	23.8	25.8	_		_	_	_
Lee et al. [25]	_	_	_	_	_		_	_	_
Lu et al. [26]	_	_	24.5	23	3.8		3.4	_	_
McNally et al. [27]	0	0	_	_	_		_	_	_
Papaconstantinou et al. [28]	0	0	22.6 ± 6.0	21.3 ± 4.1	3 4.0	0 ± 2.0	3.8 ± 1.6	9.3 ± 4.4	9.3 ± 5.0
Wolthuis et al. [29]	0	0	17	18	_		_	_	_
Adair et al. [30]	_	_	_	_	_		_	_	_
Gandhi et al. [31]	_	_	_	_	_		_	_	_
Waters et al. [32]	0	0	18	18	_		_	_	_
Keshava et al. [33]	0	0	_	_	_		_	_	_
Lim et al. [34]	_	_	_	_	3.6	± 2.3	3.9 ± 2.2	10.5 ± 7.2	11.2 ± 5.4
Khayat et al. [35]	0	0	_	_	_		_	_	_
Total or mean	0	0	23.20	23.12	3.4	.3	3.56	13.01	11.35
References		Distal free ma	rgin (cm)	Dis	sected ly	mph nodes	8	Carcinoma rec	urrence
		SILC	MLC	SIL	С	ML	.C	SILC	MLC
Chew et al. [6]		6.5	6.0	19		18		_	-
Kwag et al. [7]		7.5 ± 2.5	9.2 ± 4.0	19.0	5 ± 10.7	20.	8 ± 7.7	-	-
Pedraza et al. [8]		-	-	21.4	4 ± 8.4	19.	2 ± 7.6	-	-
Vasilakis et al. [9]		_	_	-		-		_	-
Yun et al. [10]		16.6 ± 6.2	15.8 ± 7.6	24	± 11	27	± 13	6/66	3/93
Currò et al. [11]		15.5	13.0	-		-		-	-
Egi et al. [12]		-	_	25		24		-	-
Fujii et al. [13]		9.5 ± 3.6	7.6 ± 4.1	15.0)	16.	5	_	-
Gaujoux et al. [14]		-	_	19.9	9 ± 5.2	23.	3 ± 11.5	_	_
Huscher et al. [15]		8 ± 7	6 ± 4	14.:	5	-		1/16	1/16
Katsuno et al. [16]		-	_	18	± 6	16	± 5	_	-
Osborne et al. [17] –		_	20.3	3 ± 4.2	19.	4 ± 2.6	-	-	

Table 4 continued

References	Distal free marg	gin (cm)	Dissected lymp	h nodes	Carcinoma recurrence		
	SILC	MLC	SILC	MLC	SILC	MLC	
Poon et al. [18]	5.5	6.0	-	_	-	_	
Ramos-Valadez et al. [19]	_	_	16	20	_	_	
Velthuis et al. [20]	_	_	20.3 ± 3.8	18.3 ± 6.8	_	_	
Champagne et al. [21]	_	_	14.0	12.5	_	_	
Chen et al. [22]	16	13.5	19.4	21.6	_	_	
Kim et al. [23]	17.2 ± 12.3	13.0 ± 10.1	19.5	19	_	_	
Lai et al. [24]	_	_	29.3 ± 16	23.2 ± 15.4	_	_	
Lee et al. [25]	_	_	14.5	14.5	_	_	
Lu et al. [26]	_	_	_	_	_	_	
McNally et al. [27]	_	_	8.8 ± 6.6	8.8 ± 6.6	_	_	
Papaconstantinou et al. [28]	10.5 ± 6.1	9.3 ± 4.4	15	17	2	2	
Wolthuis et al. [29]	_	_	18 ± 6	17 ± 12	0	0	
Adair et al. [30]	_	_	12	14	_	_	
Gandhi et al. [31]	_	_	20.1 ± 11.3	18.6 ± 4.1	_	_	
Waters et al. [32]	_	_	24.6 ± 12.3	18.6 ± 5.7	_	_	
Keshava et al. [33]	_	_	17	17	_	_	
Lim et al. [34]	6.6 ± 5.8	5.5 ± 5.0	23.2 ± 12.3	27.4 ± 15.8	_	_	
Khayat et al. [35]	_	_	15 ± 8	_	_	-	
Total or mean	10.98	12.26	18.59	18.82	9 (0.84 %)	6 (0.24 %)	

SILC single-incision laparoscopic colectomy, MLC multiport laparoscopic colectomy

group and 3.3 % in the MLC group (OR 0.56, 95 % CI 0.21–1.54, P = 0.26; no heterogeneity was found for $I^2 = 0$ %; P = 0.73).

Subgroup analysis: studies including low anterior resections

Two retrospective cohort studies [23, 34] reported outcomes for patients who underwent a low anterior resection (LAR). LAR represented only 20.6 % of the total number of procedures analyzed in the SILC group and 49.6 % of those in the MLC group. Morbidity rate was similar when comparing the two techniques: 25.6 % of cases in the SILC group and 23.1 % cases in the MLC (OR 0.82, 95 % CI 0.49–1.38, P = 0.46; no heterogeneity was found for $I^2 = 0$ %; P = 0.82). No significant difference was found when analyzing the outcomes: postoperative hospital stay (SMD, -0.27, 95 % CI -0.83 to 0.08, P = 0.11; heterogeneity was found for $I^2 = 76$ %; P = 0.04), and bowel function recovery (SMD, -0.22, 95 % CI -0.65 to 0.21, P = 0.31; heterogeneity was found for $I^2 = 74 \%$; P = 0.05). Conversely, the length of the distal free margin was significantly longer in the MLC group (SMD 1.78, 95 % CI 0.18 to 3.39, P = 0.03; no heterogeneity was found for $I^2 = 59$ %; P = 0.12). The mean intraoperative blood loss was impossible to meta-analyze for this subgroup of patients.

Publication bias

Funnel plots demonstrated moderate asymmetry for operative time and length of skin incision, suggesting the possibility of publication bias for these outcomes (Fig. 11). No points fell outside of the 95 % confidence interval limits for any other outcome of interest, suggesting the absence of publication bias.

Discussion

There has been a surgical evolution from open to conventional laparoscopic colorectal surgery for treatment of both benign and malignant diseases in most tertiary referral centers. In recent years, SILC has been an attractive and fascinating technique for surgeons willing to further improve laparoscopic operations. However, the role of the single-incision approach in colorectal surgery is still a matter of debate, as no conclusive data exist regarding short-term and long-term outcomes of the procedure.

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		SILC			MLC			Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Kim et al. 2011	33.4	30.3	73	17.9	20.5	106	20.2%	0.62 [0.31, 0.92]	2011	•
Papaconstantinou et al. 2011	9.3	4.4	26	9.3	5	26	13.2%	0.00 [-0.54, 0.54]	2011	+
Fujii et al. 2012	8.8	2.4	23	8.5	3.9	23	12.4%	0.09 [-0.49, 0.67]	2012	+
Yun et al. 2013	14.4	8.4	66	15	7.8	93	19.8%	-0.07 [-0.39, 0.24]	2013	+
Kwag et al. 2013	11.2	3.9	24	11.4	4.1	48	14.6%	-0.05 [-0.54, 0.44]	2013	+
Lim et al. 2014	10.5	7.2	44	11.2	5.4	263	19.7%	-0.12 [-0.44, 0.20]	2014	4
Total (95% CI)			256			559	100.0%	0.09 [-0.19, 0.37]		•
Heterogeneity: $Tau^2 = 0.08$; Cl	$hi^2 = 14$.58, df	f = 5 (P	= 0.01	1); $ ^2 =$	66%			F	-10 -5 0 5 10
Test for overall effect: $Z = 0.6$	5 (P = 0)	.53)								Favours [SILC] Favours [MLC]

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		SILC			MLC			Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	Year	IV, Fixed, 95% CI
Kim et al. 2011	17.2	12.3	73	13	10.1	106	25.6%	0.38 [0.08, 0.68]	2011	-
Papaconstantinou et al. 2011	10.5	6.1	26	9.3	4.4	26	7.8%	0.22 [-0.32, 0.77]	2011	+
Fujii et al. 2012	9.5	3.6	23	7.6	4.1	23	6.7%	0.48 [-0.10, 1.07]	2012	
Huscher et al. 2012	8	7	16	6	4	16	4.7%	0.34 [-0.36, 1.04]	2012	+
Kwag et al. 2013	7.5	2.5	24	9.2	4	48	9.4%	-0.47 [-0.97, 0.03]	2013	-
Yun et al. 2013	16.6	6.2	66	15.8	7.6	93	23.2%	0.11 [-0.20, 0.43]	2013	+
Lim et al. 2014	6.6	5.8	44	5.5	5	263	22.6%	0.21 [-0.11, 0.53]	2014	+
Total (95% CI) Haterogeneity: Chi ² - 9,71, df	- 6 (P -	- 0 14)	272	8%		575	100.0%	0.19 [0.04, 0.35]		•
Test for overall effect: $Z = 2.49$	P = 0 (P = 0.	.01)		070						-10 -5 0 5 10 Favours [SILC] Favours [MLC]

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	- 4	

		SILC			MLC		5	Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	Year	IV, Random, 95% CI
Gandhi et al. 2010	20.1	11.3	24	18.6	4.1	24	5.9%	0.17 [-0.39, 0.74]	2010	-
Waters et al. 2010	24.6	12.3	16	18.6	5.7	27	5.0%	0.68 [0.04, 1.31]	2010	
McNally et al. 2011	8.8	6.6	27	8.8	6.6	46	7.2%	0.00 [-0.48, 0.48]	2011	+
Lai et al. 2011	29.3	16	14	23.2	15.4	12	3.8%	0.38 [-0.40, 1.15]	2011	
Wolthuis et al. 2011	18	6	14	17	12	14	4.1%	0.10 [-0.64, 0.84]	2011	+
Velthuis et al. 2012	20.3	3.8	50	18.3	6.8	50	8.6%	0.36 [-0.03, 0.76]	2012	-
Osborne et al. 2012	20.3	4.2	55	19.4	2.6	327	11.0%	0.31 [0.03, 0.60]	2012	+
Katsuno et al. 2012	18	6	100	16	5	100	11.2%	0.36 [0.08, 0.64]	2012	-
Gaujoux et al. 2012	19.9	5.2	25	23.3	11.5	50	7.1%	-0.34 [-0.82, 0.14]	2012	
Yun et al. 2013	24	11	66	27	13	93	10.3%	-0.24 [-0.56, 0.07]	2013	-
Pedraza et al. 2013	21.4	8.4	50	19.2	7.6	50	8.7%	0.27 [-0.12, 0.67]	2013	
Kwag et al. 2013	19.6	10.7	24	20.8	7.7	48	7.0%	-0.13 [-0.63, 0.36]	2013	-
Lim et al. 2014	23.2	12.3	44	27.4	15.8	263	10.2%	-0.27 [-0.59, 0.05]	2014	-
Total (95% CI) Heterogeneity: Tau ² = Test for overall effect:	0.05; 0 Z = 1.1	Chi ² = 2 9 (P =	509 25.53, 0.23)	df = 12	(P = (1104 0.01); l ⁱ	100.0% ² = 53%	0.11 [-0.07, 0.28]		-10 -5 0 5 10 Favours [SILC] Favours [MLC]

Fig. 6 Meta-analysis of pathology outcomes. A Proximal free margin; B distal free margin; C harvested lymph nodes

The outcome measures of our systematic review with meta-analysis showed that there was no statistically significant difference in terms of mortality, overall and specific morbidity, and operative time when comparing the SILC patient group with the MLC patient group.

Likewise, when evaluating the oncological adequacy of SILC, the results were similar in both SILC and MLC groups. Four of the secondary outcomes significantly favored the SILC group over the MLC group: Mean intraoperative blood loss was significantly lower using the SILC procedure (75.06 vs. 91.45 ml, P = 0.03); bowel function recovered significantly earlier in the SILC patients (1.96 vs. 2.15, P = 0.03); mean postoperative hospital stay was significantly shorter in the SILC group than in the MLC group (5.55 vs. 6.60, P = 0.0005); and length of skin incision was significantly shorter in the SILC group than in

the MLC patients (3.98 vs. 5.28, P = 0.01). In contrast, our meta-analysis demonstrated that the MLC was superior to the SILC procedure for length of the distal free margin (12.26 vs. 10.98 cm, P = 0.01).

Our results confirm the hypothesis in much of the current literature that SILC is safe and feasible for the treatment of benign and malignant colorectal diseases, with short-term results comparable to that of MLC. When calculating the primary outcome measures for our research, no heterogeneity was found across the included studies for mortality rate, overall morbidity, and specific complications. In contrast, the proximal and distal free margin, and harvested lymph nodes, showed a degree of heterogeneity. Conversely, specific postoperative results included in the secondary outcomes were significantly better in the SILC group than in the MLC group, even when evidence of heterogeneity was observed.

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References	Operative time (m	in)	Previous abdomina	l surgery	Conversion to la	parotomy	Conversion to
	SILC	MLC	SILC	MLC	SILC	MLC	SILC
Chew et al. [6]	95	100	2	18	2	7	3
Kwag et al. [7]	251 ± 50	237 ± 49	2	4	0	0	7
Pedraza et al. [8]	127.9 ± 37.6	126.7 ± 63.6	24	29	0	1	5
Vasilakis et al. [9]	175.5 ± 40.2	178.7 ± 50.7	7	7	2	1	0
Yun et al. [10]	131 ± 27	143 ± 54	13	23	1	5	0
Currò et al. [11]	170	160	I	I	0	0	I
Egi et al. [12]	192.0	222.0	2	З	0	1	0
Fujii et al. [13]	174 ± 37	179 ± 40	6	4	0	1	1
Gaujoux et al. [14]	130	180	5	12	0	1	1
Huscher et al. [15]	147 ± 61	129 ± 46	I	I	0	0	1
Katsuno et al. [16]	146.3 ± 39	149.3 ± 49	I	I	0	0	1
Osborne et al. [17]	79 ± 37	113 ± 44	I	I	0	3	2
Poon et al. [18]	155	124	7	8	0	0	0
Ramos-Valadez et al. [19]	159.2 ± 29.9	162.1 ± 40.3	10	8	0	0	1
Velthuis et al. [20]	76	112	I	1	0	0	2
Champagne et al. [21]	103.8	134.4	8	7	1	1	4
Chen et al. [22]	175	165	I	1	1	0	2
Kim et al. [23]	274	254	15	25	1	3	0
Lai et al. [24]	120	135	I	I	0	0	0
Lee et al. [25]	135 ± 31	134 ± 39	I	I	4	0	2
Lu et al. [26]	180	185	I	I	0	0	0
McNally et al. [27]	114	135	12	22	0	6	5
Papaconstantinou et al. [28]	144 ± 44	144 ± 51	4	4	0	1	3
Wolthuis et al. [29]	75	83	Ι	I	0	0	0
Adair et al. [30]	139 ± 29.7	134 ± 32.3	0	0	0	0	2
Gandhi et al. [31]	143.2 ± 37.2	112.8 ± 44.8	10	12	0	0	3
Waters et al. [32]	106	100	7	10	0	0	0
Keshava et al. [33]	I	Ι	I	I	0	1	0
Lim et al. [34]	185.0 ± 47.5	139.2 ± 36.9	6	39	0	0	4
Khayat et al. [35]	Ι	I	6	118	3	45	10
Total or mean	147.28	148.97	152 (14.23 %)	353 (14.50 %)	15 (1.40 %)	76 (3.12 %)	49 (4.58 %)

Table 5 Operative results

Mathematication Respiration Respiration Respiration Respiration Reference RIC MIC SIC MIC SIC MIC Cove et al. [5] $-$ manoperative stored (1) 133 ± 28 144 ± 23 2 1 34 ± 11 7.3 ± 16 Kong et al. [7] 133 ± 28 144 ± 23 2 1 2 4 4 Vanishies et al. [8] 144 ± 23 81 ± 549 0 4 4 5 5 4 Vanishies et al. [10] 35 81 ± 549 0 0 2 4 4 5 5 4 4 5 5 4 4 5				f				1
MIC Reage et al [8] $$	Keterences	Intraoperative bloo	d loss (ml)	Reoperation		Length of skin inc	(cm) (cm)	
Check et al. (c) $ -$		SILC	MLC	SILC	MLC	SILC	MLC	1
Song et al. [7] 135 ± 33 14 ± 23 2 1 34 ± 11 73 ± 16 Pedrator at [8] 644 ± 647 872 ± 803 1 2	Chew et al. [6]	I	I	I	I	5	9	1
Refraz et al. [8] 644 ± 647 872 ± 89.8 12Variatives et al. [9] 745 ± 553 813 ± 54.9 000 90 ± 1.9 51 ± 1.9 Variatives et al. [10] -7 -75 ± 553 813 ± 54.9 00 -6 49 ± 1.9 51 ± 1.9 Curb et al. [11] 35 50 215 0 0 0 313 ± 122 55 ± 2.44 Guivos et al. [12] 9 ± 9 109 ± 99 100 ± 291 0 0 233 ± 122 55 ± 2.44 Guivos et al. [13] 9 ± 9 009 ± 291 00 ± 23 -7 -7 -7 -7 Guivos et al. [13] 200 ± 23 0 0 0 23 ± 1.2 55 ± 2.44 Guivos et al. [13] 20 ± 221 300 ± 23 -7 -7 -7 -7 Resolve et al. [13] 20 ± 221 300 ± 23 0 0 0 2.5 -7 -7 Resolve et al. [13] 20 ± 221 300 ± 23 0 0 0 0 -7 -7 -7 Poor et al. [13] 20 ± 221 00 ± 23 0 0 0 0 -7 -7 -7 Poor et al. [23] 53 ± 343 89 ± 32.1 0 0 0 -7 -7 -7 Poor et al. [23] 20 ± 23 20 ± 23 0 0 0 -7 -7 -7 Poor et al. [23] 20 ± 23 20 ± 23 20 ± 23 20 ± 23 20 ± 23 -7 -7 -7 Poor et al	Kwag et al. [7]	135 ± 28	144 ± 22	2	1	3.4 ± 1.1	7.3 ± 1.6	
Valuation (1) $(1,3)$ <	Pedraza et al. [8]	64.4 ± 64.7	87.2 ± 89.8	1	2	I	I	
Nue et al. (10)Curvo et al. (11)3555555555555555Figi et al. (13)9 ± 9 109 ± 391 0033 ± 12 555555Figi et al. (13)9 ± 9 109 ± 391 00033 ± 12 555555Figi et al. (13)9 ± 9 100 ± 391 000033 ± 12 555524Rustor et al. (15)20 ± 21 300 ± 23 22222222Rustor et al. (13)20 ± 21 300 ± 23 22222222Rustor et al. (17)025222222222Rustor et al. (17)025222222222Rustor et al. (18)53 ± 343 98 ± 521 000002222Rustor et al. (17)022222222222Rustor et al. (18)53 ± 343 98 ± 521 000000002222Rustor et al. (23)55555555552222222222 <td< td=""><td>Vasilakis et al. [9]</td><td>74.5 ± 55.3</td><td>81.3 ± 54.9</td><td>0</td><td>0</td><td>4.9 ± 1.9</td><td>5.1 ± 1.9</td><td></td></td<>	Vasilakis et al. [9]	74.5 ± 55.3	81.3 ± 54.9	0	0	4.9 ± 1.9	5.1 ± 1.9	
Curve or al. [11]3550 $ 4.3$ 4.5 Egret al. [12] 8.0 51.5 0 0 0 3.3 ± 1.2 5.5 ± 2.4 Egret al. [13] 9 ± 9 009 ± 301 0 0 0 3.3 ± 1.2 5.5 ± 2.4 Gaujox et al. [15] 2.200 $ 0$ 0 0 3.3 ± 1.2 5.5 ± 2.4 Bascher et al. [15] 2.00 $ 0$ 0 0 0 3.3 ± 1.2 5.5 ± 2.4 Bascher et al. [16] 2.92 ± 2.1 30.0 ± 2.3 $ -$ Kanon et al. [16] 2.92 ± 2.1 30.0 ± 2.3 200 0 0 0 0 $-$ Kanon et al. [17] $ -$ Romover al. [18] $50.\pm2.1$ $9.95.2.1$ 0 0 0 0 0 $ -$ Romover al. [29] $ -$ Romover al. [21] $ -$ Romover al. [23] $53\pm3.43.3$ 989 ± 5.21 0 0 0 $ -$ <td>Yun et al. [10]</td> <td>I</td> <td>I</td> <td>I</td> <td>I</td> <td>I</td> <td>I</td> <td></td>	Yun et al. [10]	I	I	I	I	I	I	
Egi et al. [2]48.051.5003.05.0Fuji et al. [3] 9 ± 9 100 ± 391 00 33 ± 12 55 ± 24 Fuji et al. [13] 9 ± 9 100 ± 301 00 33 ± 12 55 ± 24 Fusiver et al. [17] 200 ± 23 $ -$ Assume et al. [17] 200 ± 23 $ -$ Assume et al. [17] $ -$ Osborne et al. [17] $ -$ Assume et al. [17] $ -$ Osborne et al. [17] $ -$ Osborne et al. [18] 53 ± 343 589 ± 52.1 00 ± 0 0 $ -$ Osborne et al. [20] $ -$ Champare et al. [21] $ -$ Champare et al. [22] 55 ± 343 589 ± 52.1 0 0 $ -$ Champare et al. [23] $ -$ Champare et al. [23] $ -$ Champare et al. [23] $ -$ Lace et al. [24] $-$	Currò et al. [11]	35	50	I	I	4.3	4.5	
Fujir et al. [3] 9 ± 9 109 ± 391 0 0 3.3 ± 1.2 5.5 ± 2.4 Haskree al. [13] 100 90 0 0 0 2.5 5.5 ± 2.4 Haskree al. [13] 100 90 0 0 0 0 2.5 5.5 ± 2.4 Haskree al. [13] 100 90 20 2 2 $ -$ Asimove et al. [17] $ 2$ 2.6 $ -$ Poor et al. [18] 30.3 ± 3.3 89.9 ± 32.1 0 0 0 $ -$ Poor et al. [19] 53.3 ± 3.3 89.9 ± 32.1 0 0 0 $ -$ Poor et al. [21] $ -$ Por et al. [23] 53.2 ± 3.43 89.9 ± 32.1 0 0 0 $ -$ Champer et al. [23] $ -$ Champer et al. [23] 23.2 418 $ -$ Champer et al. [23] 23.2 $ -$ Lie et al. [23] 23.2 418 $ -$ Lie et al. [23] $ -$ Lie et al. [23] $ -$ Lie et al. [Egi et al. [12]	48.0	51.5	0	0	3.0	5.0	
Gaujoux et al. [14] 100 90 0 2.5 2. Huscher et al. [15] 200 $ 0$ 1 $ -$ Kassno et al. [16] 22.4 ± 1 30.0 ± 3 $ -$ Osbone et al. [17] $ -$ Poon et al. [18] $50.0 \pm 33.4.3.3$ $98.9 \pm 32.1.1$ 0 0 $ -$ <td>Fujii et al. [13]</td> <td>6 ± 6</td> <td>109 ± 391</td> <td>0</td> <td>0</td> <td>3.3 ± 1.2</td> <td>5.5 ± 2.4</td> <td></td>	Fujii et al. [13]	6 ± 6	109 ± 391	0	0	3.3 ± 1.2	5.5 ± 2.4	
Huscher et al. [5]200 $-$ 01 $ -$	Gaujoux et al. [14]	100	06	0	0	2.5	I	
Katsmo et al. [6] 22 ± 21 300 ± 23 $ -$ <t< td=""><td>Huscher et al. [15]</td><td>200</td><td>I</td><td>0</td><td>1</td><td>I</td><td>I</td><td></td></t<>	Huscher et al. [15]	200	I	0	1	I	I	
Osborne et al. [17]226Poon et al. [18]5080000Poon et al. [19]53 ± 34.389 ± 52.10003.3 ± 0.8Ramos/valadez et al. [20]Champale et al. [21]Champale et al. [23]7550Champale et al. [23]7530Kim et al. [23]7530Lat et al. [24]Lat et al. [24]Lat et al. [26]3550000000Lat et al. [26]3557418<	Katsuno et al. [16]	29.2 ± 21	30.0 ± 23	I	I	I	I	
Poon et al. [8]508000 $ -$ Ramos-Valadez et al. [9]58.3 ± 34.398.9 ± 52.100 3.3 ± 0.8 $-$ Velthis et al. [20] $ -$ Velthis et al. [21] 5.3 ± 34.3 98.9 ± 52.100 0 3.3 ± 0.8 $-$ Velthis et al. [22] 5.3 ± 34.3 98.9 ± 52.100 $ -$ Chen appage et al. [22] 5.5 50 $ -$ Chen at al. [23] 2.82 418 $ -$ Chen at al. [24] $ -$ Lie et al. [25] 2.82 418 $ -$ Lie et al. [26] 5.6 $ -$ Lie et al. [27] 50 0 0 0 0 $ -$ Lie et al. [29] $ -$ Lie et al. [29] 50 50 0 0 0 0 $ -$ Lie et al. [29] $ -$ Lie et al. [29] 57.40 87.40 87.40 87.40 87.40 $-$ Moltinis et al. [29] $ -$ <t< td=""><td>Osborne et al. [17]</td><td>I</td><td>I</td><td>2</td><td>26</td><td>I</td><td>I</td><td></td></t<>	Osborne et al. [17]	I	I	2	26	I	I	
Ramos-Valadez et al. [9] 83.3 ± 34.3 98.9 ± 52.1 0 0 3.3 ± 0.8 $-$ Velhuis et al. [20] $ +$ 6 $ -$ Champagne et al. [21] $ -$ Champagne et al. [22] 75 50 $ -$ Champagne et al. [23] $ -$ Chan et al. [23] $ -$ Kim et al. [23] $ -$ Kim et al. [23] $ -$ Kim et al. [24] $ -$ La et al. [26] 35 50 0 0 0 $ -$ Lu et al. [26] 35 50 0 0 0 $ -$ Lu et al. [26] 35 50 50 0 0 0 $ -$ Nothuis et al. [29] 57 ± 40 87 ± 70 $ -$ Pageonstantinou et al. [28] 57 ± 40 87 ± 70 $ -$ Mothuis et al. [29] $ -$ </td <td>Poon et al. [18]</td> <td>50</td> <td>80</td> <td>0</td> <td>0</td> <td>I</td> <td>I</td> <td></td>	Poon et al. [18]	50	80	0	0	I	I	
Velthuis et al. [20]46Champage et al. [21]3.84.5Champage et al. [22]75503.84.5Chen et al. [23]2824184Lat et al. [24]Lat et al. [25]282418Lat et al. [25]Le et al. [25]00Le et al. [26]355000NcNally et al. [27]5050111McNally et al. [27]5050111NcNally et al. [29]0111McNally et al. [29]0111NcNubuis et al. [29]0111McNubuis et al. [29]00111Multuris et al. [29]0100331.16.6 \pm 2.1 <td< td=""><td>Ramos-Valadez et al. [19]</td><td>58.3 ± 34.3</td><td>98.9 ± 52.1</td><td>0</td><td>0</td><td>3.3 ± 0.8</td><td>I</td><td></td></td<>	Ramos-Valadez et al. [19]	58.3 ± 34.3	98.9 ± 52.1	0	0	3.3 ± 0.8	I	
Champage et al. [21]3.84.5Champage et al. [22]755044Chen et al. [23]28241844Chen et al. [24]28241844Lai et al. [24]00Lai et al. [24]000Lai et al. [25]35500004.07 ± 1.186.4 ± 2.4La et al. [26]35500004.07 ± 1.186.4 ± 2.4McNally et al. [27]5050000Papeonsantinou et al. [28]577 ± 4087 ± 7011Nothuis et al. [29]011055555Mothuis et al. [29]011055555Mothuis et al. [29]010005555Mothuis et al. [29]010005555Mothuis et al. [29]010005555Mothuis et al. [29]555555555Mothuis et al. [30]555555555 <td>Velthuis et al. [20]</td> <td>I</td> <td>I</td> <td>4</td> <td>6</td> <td>I</td> <td>I</td> <td></td>	Velthuis et al. [20]	I	I	4	6	I	I	
Chen et al. [2]755044Kin et al. [23]282418Lai et al. [23]282418Lai et al. [24]000Lai et al. [25]000La et al. [26]35500004.07 ±1.184.77 ±1.194.77 ±1.19McNaly et al. [27]5050000Papaconstantinou et al. [28]57 ± 4087 ± 7011Nothius et al. [29]00111Adair et al. [30]103.3 ±1.16.6 ±2.1Mothius et al. [30]6.25 ± 37.690.6 ± 60.6003.3 ±1.16.6 ±2.1Waters et al. [33]Waters et al. [33]Water et al. [33]<	Champagne et al. [21]	I	I	I	I	3.8	4.5	
Kim et al. [23]282418La et al. [24]00La et al. [25]0005.1 \pm 1.86.4 \pm 2.4Le et al. [25]0005.1 \pm 1.86.4 \pm 2.4Lu et al. [26]35500004.07 \pm 1.184.77 \pm 1.19McNally et al. [27]5050111Papaconstantiou et al. [29]57 \pm 4087 \pm 70Papaconstantiou et al. [29]0111McNubis et al. [29]0101003.85.1Molthuis et al. [29]001003.85.1Molthuis et al. [29]001003.85.1Molthuis et al. [31]6.25 \pm 37.690.6 \pm 60.60003.3 \pm 1.16.6 \pm 2.1Waters et al. [32]54900001Mater et al. [33]4.136.5 \pm 3.75.05.05.05.0Mater et al. [34]	Chen et al. [22]	75	50	I	I	4	4	
Lai et al. $[24]$ 00Le et al. $[25]$ 005.1 \pm 1.86.4 \pm 2.4Le et al. $[25]$ 35500005.1 \pm 1.86.4 \pm 2.4Lu et al. $[27]$ 5050111McNally et al. $[27]$ 5050111Papaconstantiou et al. $[28]$ 57 \pm 4087 \pm 70Papaconstantiou et al. $[29]$ 01010Molthuis et al. $[29]$ 01010555Adair et al. $[30]$ 103.3 \pm 1.16.6 \pm 2.16.6 \pm 2.1Molthuis et al. $[31]$ 6.2 5 \pm 37.690.6 \pm 60.6003.3 \pm 1.16.6 \pm 2.16.6 \pm 2.1Waters et al. $[32]$ Waters et al. $[33]$ 4.7 \pm 0.85.05.0Lim et al. $[34]$ 82.3 \pm 45.87.0.1 \pm 48.3Lim et al. $[35]$ 4.7 \pm 0.85.0Lim et al. $[35]$ Kayaya et al. $[35]$ Lim et al. $[35]$ </td <td>Kim et al. [23]</td> <td>282</td> <td>418</td> <td>I</td> <td>I</td> <td>I</td> <td>I</td> <td></td>	Kim et al. [23]	282	418	I	I	I	I	
Lee et al. [25]005.1 ± 1.8 6.4 ± 2.4 Lu et al. [26]3550004.07 ± 1.184.77 ± 1.19McNally et al. [27]505011McNally et al. [27]505011Papaconstantion et al. [28]57 ± 4087 ± 70Papaconstantion et al. [29]01010Volthuis et al. [29]0101055Adair et al. [30]Adair et al. [31]6.25 ± 37.690.6 ± 60.6003.3 ± 1.16.6 ± 2.1Maters et al. [32]54900103.3 ± 1.16.6 ± 2.1Waters et al. [33]Waters et al. [33]4.7 ± 0.85.1Kashava et al. [33]Lim et al. [34]82.3 ± 45.870.1 ± 48.3Khayat et al. [35]Lim et al. [34]82.3 ± 45.870.1 ± 48.3Khayat et al. [35]Total or mean75.0691.4512 (1.38 %)3.8 (2.75 %)5.08Start12 (1.38 %)3.8 (2.75 %)3.985.28	Lai et al. [24]	I	I	0	0	I	I	
Lu et al. [26]35500004.07 \pm 1.184.77 \pm 1.19McNally et al. [27]50505011 $ -$ Papaconstantinou et al. [28] 57 ± 40 87 ± 70 $ -$ Papaconstantinou et al. [29] 57 ± 40 87 ± 70 $ -$ Wolthuis et al. [29] 0 10 1 0 1 0 5 5 Wolthuis et al. [30] $ -$ Adair et al. [31] 62.5 ± 37.6 90.6 ± 60.6 0 0 0 3.3 ± 1.1 6.6 ± 2.1 Waters et al. [32] 5.4 90.6 ± 60.6 0 0 1 $ -$ Waters et al. [33] 5.4 90.6 ± 60.6 0 0 1 $ -$ Waters et al. [33] 5.4 90.6 ± 60.6 0 0 1 $ -$ Waters et al. [33] 5.4 90.6 ± 60.6 0 0 1 $ -$ Waters et al. [33] 5.1 $ -$ Keshava et al. [34] 82.3 ± 45.8 70.1 ± 48.3 $ -$ Lim et al. [35] $ -$ Khavat et al. [35] $ -$ <	Lee et al. [25]	I	I	0	0	5.1 ± 1.8	6.4 ± 2.4	
McNally et al. [27]505011Papaconstantinu et al. [28] 57 ± 40 87 ± 70 Papaconstantinu et al. [29]01010555Wolthuis et al. [20]Molthuis et al. [30]1010555Adair et al. [30]103.85.1Gandhi et al. [31] 62.5 ± 37.6 90.6 ± 60.6 0003.3 \pm 1.16.6 \pm 2.1Waters et al. [32]5490001Waters et al. [33]4.35.0Lim et al. [34] 82.3 ± 45.8 70.1 \pm 48.34.7 \pm 0.84.5 \pm 0.7Khayat et al. [35]3.9 \pm 2.5Total or mean75.0691.4512(1.38 %)3.8 (2.75 %)3.985.28	Lu et al. [26]	35	50	0	0	4.07 ± 1.18	4.77 ± 1.19	
Papaconstantinou et al. [28] 57 ± 40 87 ± 70 $ -$ Wolthuis et al. [29]0101055Mair et al. [30] $ -$ 103.8Adair et al. [30] $ 1$ 03.8Adair et al. [31] 62.5 ± 37.6 90.6 ± 60.6 00 3.3 ± 1.1 6.6 ± 2.1 Gandhi et al. [31] 62.5 ± 37.6 90.6 ± 60.6 00 3.3 ± 1.1 6.6 ± 2.1 Waters et al. [32] 5.4 90 001 $ -$ Waters et al. [33] $ -$ Keshava et al. [33] $ -$ Kustava et al. [33] $ -$ Kustava et al. [33] $ -$ Kustava et al. [34] 82.3 ± 45.8 70.1 ± 48.3 $ -$ Khyat et al. [35] $ -$ Khyat et al. [35] $ -$ Koto 70.6 91.45 $12(1.38 \%)$ $38(2.75 \%)$ 3.98 5.28	McNally et al. [27]	50	50	1	1	I	I	
Wolthuis et al. [29]0101055Adair et al. [30]103.85.1Adair et al. [30]103.85.1Gandhi et al. [31] 62.5 ± 37.6 90.6 ± 60.6 003.3 \pm 1.1 6.6 ± 2.1 Waters et al. [31] 5.4 90 01Waters et al. [32]4.35.0Keshava et al. [33]4.35.0Lim et al. [34]82.3 \pm 45.870.1 \pm 48.34.7 \pm 0.8 4.5 ± 0.7 Khaya et al. [35]Lim et al. [35]3.9 \pm 2.5Total or mean75.0691.4512 (1.38 %)38 (2.75 %)3.985.28	Papaconstantinou et al. [28]	57 ± 40	87 ± 70	I	I	I	I	
Adair et al. [30]103.85.1Gandhi et al. [31] 62.5 ± 37.6 90.6 ± 60.6 003.3 \pm 1.1 6.6 ± 2.1 Waters et al. [32] 54 90.6 ± 60.6 001Waters et al. [32] 54 90.6 ± 60.6 001Waters et al. [32] 54 90 001Keshava et al. [33]4.35.0Lim et al. [34] 82.3 ± 45.8 70.1 ± 48.3 4.7 \pm 0.8 4.5 ± 0.7 Khaya et al. [35]Yotal or mean75.06 91.45 $12(1.38 \%)$ $38(2.75 \%)$ 3.98 5.28	Wolthuis et al. [29]	0	10	1	0	5	5	
Gandhi et al. [31] 62.5 ± 37.6 90.6 ± 60.6 0 0 0 3.3 ± 1.1 6.6 ± 2.1 Waters et al. [32] 54 90 0 1 $ -$ Keshava et al. [33] $ 4.3$ 5.0 Lim et al. [34] 82.3 ± 45.8 70.1 ± 48.3 $ 4.7 \pm 0.8$ 4.5 ± 0.7 Khaya et al. [35] $ -$ Total or mean 75.06 91.45 $12(1.38 \%)$ $38(2.75 \%)$ 3.98 5.28	Adair et al. [30]	I	I	1	0	3.8	5.1	
Waters et al. [32] 54 90 0 1 $ -$ Keshava et al. [33] $ 4.3$ 5.0 Lim et al. [34] 82.3 ± 45.8 70.1 ± 48.3 $ 4.7 \pm 0.8$ 4.5 ± 0.7 Khayat et al. [35] $ -$ Total or mean 75.06 91.45 $12(1.38 \%)$ $38(2.75 \%)$ 3.98 5.28	Gandhi et al. [31]	62.5 ± 37.6	90.6 ± 60.6	0	0	3.3 ± 1.1	6.6 ± 2.1	
Keshava et al. [33]4.35.0Lim et al. [34] 82.3 ± 45.8 70.1 ± 48.3 4.7 ± 0.8 4.5 ± 0.7 Khayat et al. [35] 3.9 ± 2.5 -Total or mean 75.06 91.45 $12(1.38\%)$ $38(2.75\%)$ 3.98 5.28	Waters et al. [32]	54	06	0	1	I	I	
Lim et al. [34] 82.3 ± 45.8 70.1 ± 48.3 4.7 \pm 0.8 4.5 ± 0.7 Khayat et al. [35]3.9 \pm 2.5-Total or mean75.0691.4512 (1.38 %)38 (2.75 %)3.985.28	Keshava et al. [33]	Ι	I	Ι	Ι	4.3	5.0	
Khayat et al. [35]3.9 \pm 2.5Total or mean75.0691.4512 (1.38 %)38 (2.75 %)3.985.28	Lim et al. [34]	82.3 ± 45.8	70.1 ± 48.3	Ι	Ι	4.7 ± 0.8	4.5 ± 0.7	
Total or mean 75.06 91.45 12 (1.38 %) 38 (2.75 %) 3.98 5.28	Khayat et al. [35]	Ι	Ι	Ι	Ι	3.9 ± 2.5	I	
	Total or mean	75.06	91.45	12 (1.38 %)	38 (2.75 %)	3.98	5.28	

Δ										
		SILC			MLC			Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Gandhi et al. 2010	143.2	37.2	24	112.8	44.8	24	6.6%	0.73 [0.14, 1.31]	2010	+
Adair et al. 2010	139	29.7	17	134	32.3	17	6.2%	0.16 [-0.52, 0.83]	2010	+
Papaconstantinou et al. 2011	144	44	26	144	51	26	6.9%	0.00 [-0.54, 0.54]	2011	+
Lee et al. 2011	135	31	46	134	39	46	7.6%	0.03 [-0.38, 0.44]	2011	+
Fujii et al. 2012	174	37	23	179	40	23	6.7%	-0.13 [-0.71, 0.45]	2012	-
Katsuno et al. 2012	146.3	39	100	149.3	49	100	8.2%	-0.07 [-0.34, 0.21]	2012	+
Huscher et al. 2012	147	61	16	129	46	16	6.0%	0.32 [-0.37, 1.02]	2012	+-
Ramos-Valadez et al. 2012	159.2	29.9	20	162.1	40.3	20	6.4%	-0.08 [-0.70, 0.54]	2012	-
Osborne et al. 2012	79	37	55	113	44	327	8.1%	-0.79 [-1.08, -0.50]	2012	+
Kwag et al. 2013	251	50	24	237	49	48	7.2%	0.28 [-0.21, 0.77]	2013	+-
Vasilakis et al. 2013	175.5	40.2	20	178.7	50.7	20	6.4%	-0.07 [-0.69, 0.55]	2013	+
Pedraza et al. 2013	127.9	37.6	50	126.7	63.6	50	7.7%	0.02 [-0.37, 0.41]	2013	+
Yun et al. 2013	131	27	66	143	54	93	8.0%	-0.27 [-0.58, 0.05]	2013	-
Lim et al. 2014	185	47.5	44	139.2	36.9	263	8.0%	1.18 [0.85, 1.52]	2014	+
Total (95% CI)			531			1073	100.0%	0.09 [-0.22, 0.39]		•
Heterogeneity: Tau ² = 0.27; Cl	$ni^2 = 88.$	10, df	= 13 (P < 0.0	0001);	$l^2 = 85$	5%			-10 -5 0 5 10
Test for overall effect: $Z = 0.56$	5 (P = 0.	58)								Favours [SILC] Favours [MLC]

В

		SILC			MLC			Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Gandhi et al. 2010	62.5	37.6	24	90.6	60.6	24	9.1%	-0.55 [-1.13, 0.03]	2010	-
Papaconstantinou et al. 2011	57	40	26	87	70	26	9.5%	-0.52 [-1.07, 0.04]	2011	
Ramos-Valadez et al. 2012	58.3	34.3	20	98.9	52.1	20	7.8%	-0.90 [-1.56, -0.25]	2012	
Katsuno et al. 2012	29.2	21	100	30	23	100	16.8%	-0.04 [-0.31, 0.24]	2012	+
Fujii et al. 2012	9	9	23	109	391	23	9.0%	-0.36 [-0.94, 0.23]	2012	
Pedraza et al. 2013	64.4	64.7	50	87.2	89.8	50	13.3%	-0.29 [-0.68, 0.11]	2013	-
Kwag et al. 2013	135	28	24	144	22	48	10.8%	-0.37 [-0.86, 0.13]	2013	
Vasilakis et al. 2013	74.5	55.3	20	81.3	54.9	20	8.3%	-0.12 [-0.74, 0.50]	2013	-
Lim et al. 2014	82.3	45.8	44	70.1	48.3	263	15.5%	0.25 [-0.07, 0.57]	2014	-
Total (95% CI)			331			574	100.0%	-0.26 [-0.48, -0.03]		•
Heterogeneity: Tau ² = 0.06; Ch	$ni^2 = 17$.01, dt	= 8 (P	= 0.03	$(3); I^2 =$	53%				
Test for overall effect: $Z = 2.23$	B (P = 0	.03)								Favours [SILC] Favours [MLC]

С

	5	SILC			MLC		1	Std. Mean Difference		Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
Gandhi et al. 2010	2.7	0.8	24	3.3	1.1	24	4.7%	-0.61 [-1.19, -0.03]	2010	
Adair et al. 2010	3.9	3.7	17	4.1	2.2	17	3.8%	-0.06 [-0.74, 0.61]	2010	+
Papaconstantinou et al. 2011	3.6	1.6	26	5	2.2	26	4.9%	-0.72 [-1.28, -0.15]	2011	-
Lee et al. 2011	4.6	1.6	46	4.3	0.8	46	7.2%	0.24 [-0.17, 0.65]	2011	+-
Kim et al. 2011	9.6	9.6	73	15.5	9.8	106	9.5%	-0.60 [-0.91, -0.30]	2011	+
Fujii et al. 2012	8.2	3.4	23	12.7	12.9	23	4.6%	-0.47 [-1.06, 0.12]	2012	
Katsuno et al. 2012	9.6	1.8	100	9.7	2.6	100	10.2%	-0.04 [-0.32, 0.23]	2012	+
Huscher et al. 2012	6	3	16	7	2	16	3.5%	-0.38 [-1.08, 0.32]	2012	+
Ramos-Valadez et al. 2012	3.2	1	20	3.8	2.1	20	4.2%	-0.36 [-0.98, 0.27]	2012	
Kwag et al. 2013	7.1	3.4	24	8.1	3.5	48	5.8%	-0.29 [-0.78, 0.21]	2013	
Vasilakis et al. 2013	3.9	1.6	20	5.5	2	20	4.0%	-0.87 [-1.52, -0.21]	2013	
Pedraza et al. 2013	4.5	3.7	50	4	1.7	50	7.6%	0.17 [-0.22, 0.57]	2013	+
Yun et al. 2013	8	4	66	9	5	93	9.2%	-0.22 [-0.53, 0.10]	2013	-
Lim et al. 2014	8.2	2.3	44	8.8	4.6	263	9.2%	-0.14 [-0.46, 0.18]	2014	+
Khayat et al. 2015	8	6	84	10	7	715	11.6%	-0.29 [-0.52, -0.06]	2015	-
Total (95% CI)			633			1567	100.0%	-0.27 [-0.42, -0.12]		•
Heterogeneity: Tau ² = 0.04; Ch	$i^2 = 26$.45, 0	if = 14	(P = 0)	.02); I ²	= 47%				-10 -5 0 5 10
Test for overall effect: Z = 3.48	(P = 0.)	0005	5)							Favours [SILC] Favours [MLC]
										the second s

Fig. 7 Meta-analysis of secondary outcomes. A Operative time; B intraoperative blood loss; C postoperative hospital stay

To the best of our knowledge, this is the fifth meta-analysis to compare the results of SILC versus MLC in colorectal surgery. Previous pooled analyses were based on 27 comparative studies and one randomized controlled trial [39], 15 comparative studies [36, 37], or 11 comparative studies [38]. The results of our meta-analysis, based on a total of 3502 laparoscopic procedures, included the largest number of adult patients from 30 comparative studies in the literature.

The need for timely summarized data regarding important clinical questions also justifies the use of pooled analysis, including observational studies, when there is a lack of randomized controlled trials. However, meta-analyses based on observational studies are more prone to bias, resulting in low-quality evidence [43].

With the exception of two RCTs [15, 18], 17 of 27 of the comparative studies included were designed as case-matched studies [6, 7, 9, 12–14, 16, 19–22, 25, 28–31, 35]. Pooling matched case–control design studies should reduce the confounding effects of covariates on the treatment results [13].

	SIL	C	MLC Odds Ratio			Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	Year	M-H, Fixed, 95% CI
McNally et al. 2011	0	27	6	46	13.2%	0.11 [0.01, 2.09]	2011	• •
Papaconstantinou et al. 2011	0	26	1	26	4.1%	0.32 [0.01, 8.24]	2011	
Chen et al. 2011	1	18	0	21	1.2%	3.69 [0.14, 96.22]	2011	
Champagne et al. 2011	1	29	1	29	2.7%	1.00 [0.06, 16.79]	2011	
Lee et al. 2011	4	46	0	46	1.2%	9.85 [0.51, 188.36]	2011	· · · · · · · · · · · · · · · · · · ·
Kim et al. 2011	1	73	3	106	6.7%	0.48 [0.05, 4.68]	2011	
Osborne et al. 2012	0	55	3	327	2.8%	0.84 [0.04, 16.39]	2012	
Egi et al. 2012	0	10	1	10	4.0%	0.30 [0.01, 8.33]	2012	
Gaujoux et al. 2012	0	25	1	50	2.7%	0.65 [0.03, 16.46]	2012	
Fujii et al. 2012	0	23	1	23	4.1%	0.32 [0.01, 8.25]	2012	
Pedraza et al. 2013	0	50	1	50	4.1%	0.33 [0.01, 8.21]	2013	
Keshava et al. 2013	0	75	1	74	4.1%	0.32 [0.01, 8.09]	2013	
Yun et al. 2013	1	66	5	93	11.3%	0.27 [0.03, 2.37]	2013	
Vasilakis et al. 2013	2	20	1	20	2.5%	2.11 [0.18, 25.35]	2013	
Chew et al. 2013	2	40	7	104	10.2%	0.73 [0.14, 3.67]	2013	
Khayat et al. 2015	3	84	45	715	25.2%	0.55 [0.17, 1.81]	2015	
Total (95% CI)		667		1740	100.0%	0.64 [0.38, 1.10]		•
Total events	15		77					
Heterogeneity: Chi ² = 8.41, df	= 15 (P =	= 0.91)	; $I^2 = 0\%$					
Test for overall effect: Z = 1.62	P = 0.1	.1)						Favours [SILC] Favours [MLC]

Fig. 8 Meta-analysis of conversion to laparotomy

	SIL	2	MLC	2	Odds Ratio Od			Odds	Odds Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	Year		M-H, Fixe	ed, 95% CI	
Adair et al. 2010	1	17	0	17	2.4%	3.18 [0.12, 83.76]	2010		3	-	
Waters et al. 2010	0	16	1	27	5.6%	0.54 [0.02, 13.93]	2010				
Wolthuis et al. 2011	1	14	0	14	2.3%	3.22 [0.12, 86.09]	2011		-		
McNally et al. 2011	1	27	1	46	3.7%	1.73 [0.10, 28.85]	2011			•	-
Huscher et al. 2012	0	16	1	16	7.5%	0.31 [0.01, 8.28]	2012				
Osborne et al. 2012	2	55	26	327	37.0%	0.44 [0.10, 1.90]	2012			<u> </u>	
Velthuis et al. 2012	4	50	6	50	28.3%	0.64 [0.17, 2.41]	2012				
Pedraza et al. 2013	1	50	2	50	10.1%	0.49 [0.04, 5.58]	2013			<u> </u>	
Kwag et al. 2013	2	24	1	48	3.1%	4.27 [0.37, 49.68]	2013			•	
Total (95% CI)		269		595	100.0%	0.79 [0.40, 1.56]			-	-	
Total events	12		38								
Heterogeneity: Chi ² =	4.75, df	= 8 (P =	= 0.78);	$l^2 = 0\%$				0.01	01	1 10	100
Test for overall effect:	Z = 0.68	(P = 0)	.50)					0.01	Favours [SILC]	Favours [MLC]	100

Fig. 9 Meta-analysis of reoperation

The majority of patients in this meta-analysis were oncology patients. The parameters used to evaluate the oncological appropriateness of the SILC procedure, such as the number of harvested lymph nodes and resection margins, were adequate in all studies included. However, there were no data regarding long-term outcomes, such as disease-free and cancer-related survival, as all the studies included were published between 2010 and 2015. For SILC to be retained as a standard procedure for the treatment of colorectal cancer, it should also be supported by favorable long-term oncological results [23].

Among the secondary outcomes that significantly favored SILC, blood loss without blood transfusion and earlier recovery of bowel function are not likely to be of clinical significance, as other authors have also reported [47]. Despite mean postoperative hospital stay being

significantly shorter in the SILC than in the MLC group (5.5 vs. 6.6 days, P = 0.005), a previously published series of conventional laparoscopic colon resection have reported a median hospital stay of 4 or 5 days [49]. The length of skin incision was significantly shorter in the SILC than in the MLC group (3.98 vs. 5.28 cm, P = 0.01). However, a bigger specimen size required a larger incision for the extraction, and thus, some authors have suggested measuring the length of the incision at the end of the operation, rather than at the beginning [50, 51]. One of the hypothetical benefits of SILC should be improved cosmesis and patient satisfaction, which are related to the final length of the skin incision. This outcome was impossible to meta-analyze because only Lee et al. [25] addressed the issue, finding cosmetic scores higher for SILC than for MLC, without any difference in body image score. Moreover, drawing a

Α

	:	SILC		MLC				Std. Mean Difference			Std. Mean Difference	2
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year		IV, Random, 95% CI	
Kim et al. 2011	2.5	1.2	73	3.2	1.8	106	23.1%	-0.44 [-0.74, -0.14]	2011		-	
Lee et al. 2011	2.6	0.9	46	3.1	0.8	46	17.7%	-0.58 [-1.00, -0.16]	2011		-	
Kwag et al. 2013	1.7	0.6	24	2.2	1.1	48	14.7%	-0.51 [-1.01, -0.02]	2013			
Yun et al. 2013	3	1	66	3	1	93	22.4%	0.00 [-0.32, 0.32]	2013		+	
Lim et al. 2014	1.9	1.1	44	1.9	1	263	22.2%	0.00 [-0.32, 0.32]	2014		+	
Total (95% CI)			253			556	100.0%	-0.28 [-0.53, -0.03]			٠	
Heterogeneity: Tau ² =	0.05; 0	Chi ² =	9.80,	df = 4	(P =	0.04); I	$ ^2 = 59\%$			-10	-5 0	5 10
Test for overall effect: $Z = 2.18$ (P = 0.03)							-10	Favours [SILC] Favours [I	VILC]			

	-	

		SILC MLC						Std. Mean Difference		Std. Mean	Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Randoi	n, 95% CI	
Gandhi et al. 2010	3.3	1.1	24	6.6	2.1	24	13.6%	-1.94 [-2.63, -1.24]	2010	+		
Lee et al. 2011	5.1	1.8	46	6.4	2.4	46	14.8%	-0.61 [-1.03, -0.19]	2011	+		
Lu et al. 2011	4.07	1.18	27	4.77	1.19	68	14.7%	-0.58 [-1.04, -0.13]	2011	-		
Fujii et al. 2012	3.3	1.2	23	5.5	2.4	23	14.0%	-1.14 [-1.77, -0.51]	2012			
Kwag et al. 2013	3.4	1.1	24	7.3	1.6	48	13.8%	-2.65 [-3.31, -1.99]	2013			
Vasilakis et al. 2013	4.9	1.9	20	5.1	1.9	20	14.0%	-0.10 [-0.72, 0.52]	2013	-	-	
Lim et al. 2014	4.7	0.8	44	4.5	0.7	263	15.1%	0.28 [-0.04, 0.60]	2014		•	
Total (95% CI)			208			492	100.0%	-0.94 [-1.65, -0.22]		•		
Heterogeneity: Tau ² =	0.86; 0	$hi^2 = 8$	85.21,	df = 6 (P < 0.	00001)); I ² = 939	6		-10 -5 (ι Į	10
Test for overall effect:	Z = 2.5	6 (P =	0.01)							Favours [SILC]	Favours [MLC]	10

Fig. 10 Meta-analysis of secondary outcomes. A Recovery of bowel function (flatus); B length of skin incision

conclusion regarding cosmetics results is not easy, as satisfaction score may be age- and gender-related, and could be irrelevant in elderly patients undergoing operations for cancer [20].

It is important to note that the number of low anterior resections performed in the SILC group was significantly lower than in the MLC group. SILC patients underwent right hemicolectomy in 56 % of cases (599 patients), whereas the percentage of low anterior resections performed in this group was only 12 % (128 patients). Conversely, patients in the MLC group underwent right hemicolectomy in 41 % of cases (998 patients), whereas a low anterior resection was performed in 25 % (609 patients).

Moreover, in our study the mean BMI of surgical patients was 24.86 in the SILC group versus 25.67 in the MLC group, with a statistically significant difference (P = 0.04). Data were insufficient to allow meaningful conclusions to be drawn regarding obese patients with a BMI > 30 kg/m². In a recent case-matched study, primarily based on patients who underwent SILC for benign disease, Keller et al. reported that SILC in obese patients had significantly longer operative times and higher blood loss, but comparable conversion rates, oncologic outcomes, lengths of stay, complication, and readmission rates as the non-obese cohorts [52].

As in colorectal surgery obesity poses additional technical challenges, safety and feasibility of SILS in obese patients remains one of the most important issues for clarification in the future. Moreover, these results point out a selection bias which may have influenced the outcomes, as the most complex operations, and probably the most "difficult patients" have been approached by MLC.

Postoperative pain score evaluation was impossible to meta-analyze because few studies addressed this issue. In the RCT by Poon et al. [18], postoperative pain score evaluated by the visual analog scale was significantly lower in the SILC group than in the MLC group, which subsequently reduced hospital stay in the SILC group. Conversely, greater wound irritation, due to insertion of all surgical instruments through a single incision, may increase the intensity of postoperative pain score after SILC procedure will be sufficiently assessed by prospective RCTs only.

Data from pooled studies were insufficient to define a learning curve after which laparoscopic surgeons can safely master SILC. In the beginning, difficulties with instruments overcrowding and triangulation can make the SILC procedure cumbersome [22, 50]. An experienced and well-trained laparoscopic surgeon will also subsequently overcome these disadvantages by the use of new and innovative instruments [29, 50].

Only three of the included studies reported results relating to the operative costs of SILC, but standard deviations were provided only by Fujii et al. [13]. Therefore, the meta-analysis for this outcome of interest could not be carried out. However, Fujii reported a statistically significant difference in the cost of access instruments between

Table 6 Postoperative outcomes 2

Author (year)	Recovery of (flatus)	bowel function	Start regula	r diet (days)	Readmission		Incisional hernia		
	SILC	MLC	SILC	MLC	SILC	MLC	SILC	MLC	
Chew et al. [6]	_	_	_	_	1	7	_	_	
Kwag et al. [7]	1.7 ± 0.6	2.2 ± 1.1	2.8 ± 1	3.6 ± 1.4	0	0	_	_	
Pedraza et al. [8]	-	-	-	-	1	2	-	-	
Vasilakis et al. [9]	-	-	-	-	1	3	-	-	
Yun et al. [10]	3 ± 1	3 ± 1	-	-	1	2	-	-	
Currò et al. [11]	2	2	-	-	-	-	-	-	
Egi et al. [12]	-	_	-	-	-	-	_	_	
Fujii et al. [13]	-	_	-	-	-	-	_	_	
Gaujoux et al. [14]	-	_	-	-	0	0	_	_	
Huscher et al. [15]	1	1	3	3	0	0	_	_	
Katsuno et al. [16]	-	_	-	-	-	-	_	_	
Osborne et al. [17]	1	1	1	1	5	15	1	6	
Poon et al. [18]	-	_	-	-	0	0	_	_	
Ramos-Valadez et al. [19]	-	_	-	-	0	0	_	_	
Velthuis et al. [20]	-	_	-	-	-	-	0	1	
Champagne et al. [21]	_	_	_	-	_	_	0	0	
Chen et al. [22]	2	2	_	_	_	_	_	_	
Kim et al. [23]	2.5 ± 1.2	3.2 ± 1.8	4.2 ± 2.9	6.5 ± 2.7	_	_	_	_	
Lai et al. [24]	-	-	0.75	0.70	0	0	-	-	
Lee et al. [25]	2.6 ± 0.9	3.1 ± 0.8	-	-	-	-	-	-	
Lu et al. [26]	-	-	-	-	0	0	-	-	
McNally et al. [27]	-	-	-	-	0	0	-	-	
Papaconstantinou et al. [28]	-	-	-	-	-	-	-	-	
Wolthuis et al. [29]	-	-	-	-	0	0	0	0	
Adair et al. [30]	-	_	-	-	0	0	_	_	
Gandhi et al. [31]	-	_	-	-	0	0	_	_	
Waters et al. [32]	_	_	_	-	1	1	_	_	
Keshava et al. [33]	-	_	-	-	_	-	_	_	
Lim et al. [34]	1.9 ± 1.1	1.9 ± 1.0	_	_	_	-	_	_	
Khayat et al. [35]	-	_	_	_	_	-	_	_	
Total or mean	1.96	2.15	2.35	2.96	10 (0.93 %)	30 (1.23 %)	1 (0.09 %)	7 (0.28 %)	

SILC single-incision laparoscopic colectomy, MLC multiport laparoscopic colectomy

the two groups. The total mean per-patient cost of access instruments was 62.761 ± 2.946 Japanese yen with SILC and 77.130 ± 7.869 Japanese yen with MLC [13]. McNally et al. [27] reported that additional cost for SILC was approximately 250 American dollar. In a study published by Waters et al. [32], the marginal increase in direct operative cost for SILC was 310–410 American dollars per case. However, the single-incision technique can reduce the number of traditional trocars used, thereby minimizing the cost gap. This data showed that the additional cost perpatient was always related to the major cost of the particular single-port used. Thus, SILC should be more costeffective than MLC when a statistically significant difference in improved postoperative recovery is demonstrated by RCTs.

Finally, a comprehensive analysis of the outcomes of interest for our research shows that the expectation of benefits using the SILC procedure must not compromise patient safety. The majority of the included studies were conducted in highly specialized laparoscopic units, and this may be a limiting factor for the extensive use of the SILC procedure in less specialized units where required expertise is unavailable [17].

In conclusion, SILC could be considered as a safe and feasible alternative to MLC in experienced hands, and in selected patients. However, due to the very



Fig. 11 Funnel plots demonstrate moderate asymmetry for length of skin incision (A) and operative time (B), suggesting the possibility of publication bias. No points fall outside of the 95 % CI limits for any other outcome of interest, suggesting the absence of publication bias

small number of single-incision low anterior resections analyzed in this systematic review, a clear indication for low rectal cancer cannot be validated. Moreover, the statistically significant lower BMI reported in the SILC group suggests the presence of selection biases within current research, which was primarily based on data from observational studies. Therefore, the results must be approached with caution. Before recommending SILC for everyday clinical practice in colorectal surgery, we believe that all aspects of the procedure should be better assessed by high-quality multicenter prospective RCTs and subsequent clustered meta-analysis, with special regard to low rectal cancers.

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Author contributions Podda M was involved in study design, acquisition, interpretation, and analysis of data; drafting and critically revising the article for important intellectual content; and final approval of the version to be published; Saba A was involved in acquisition, interpretation, and analysis of data; drafting and critically revising the article for important intellectual content; and final approval of the version to be published; Porru F was involved in interpretation and analysis of data; drafting and critically revising the article for important intellectual content; and final approval of the version to be published; Porru F was involved in interpretation and analysis of data; drafting and critically revising the article for important intellectual content; and final approval of the version to be published; Pisanu A was involved in study design, acquisition, interpretation, and analysis of data; drafting and critically revising the article for important intellectual content; and final approval of the version to be published.

Compliance with ethical standards

Disclosures Mauro Podda, Alessandra Saba, Federica Porru, and Adolfo Pisanu have no conflicts of interest or financial ties to disclose.

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