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Single-incision versus three-port laparoscopic appendectomy for acute appendicitis: systematic review and meta-analysis of randomized controlled trials

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Abstract
Background Three-port laparoscopic appendectomy (TPLA) has been shown superior to open appendectomy for acute appendicitis (AA); alternatively, single-incision laparoscopic appendectomy (SILA) is gaining popularity. The choice between SILA and traditional TPLA remains controversial. This meta-analysis of high-quality randomized controlled trials (RCTs) aims to compare efficacy and safety of SILA with TPLA for AA.
Methods We searched MEDLINE, EMBASE, and the Cochrane Library for RCTs comparing SILA with TPLA. Reference lists of relevant articles and reviews, conference proceedings, and ongoing trial databases were also searched. Primary outcomes were operative time, postoperative complications, hospital duration, and days back to normal activities. Meta-analysis was conducted where possible comparing items using weighted mean differences (WMDs) and relative risks (RRs) according to type of data. Methodological quality was evaluated to assess bias risk.
Results A total of 8 distinct RCTs comparing SILA ($n = 616$) with TPLA ($n = 618$) published from 2010 to 2013 were identified in our analysis. SILA took longer to conduct than TPLA (43 vs 38, WMD: 5.96, 95 % CI 2.54–9.38, $P = 0.0006$). Patients undergoing SILA needed more extra trocars addressed during operation (7 % vs 0 %, RR: 12.36, 95 % CI 3.83–39.90, $P < 0.0001$), but could return to full activities earlier (6 vs 7, WMD: −0.68, 95 % CI −1.10 to −0.26, $P = 0.001$). However, these differences were not clinically significant. All other parameters were comparable.
Conclusions These results provide level 1a support for the clinical similarity that SILA is basically as feasible, effective and safe as TPLA when dealing with AA, although statistically, SILA takes longer to perform, requires more extra trocars, and benefits patients with faster recovery compared with TPLA. Further RCTs are needed to update our finding with advancement of surgical techniques and skills.

Keywords Single-incision laparoscopic appendectomy · Three-port laparoscopic appendectomy · Acute appendicitis · Efficacy · Safety

Open appendectomy has been considered standard treatment for acute appendicitis (AA) since first described by McBurney [1] in 1894. Recently, meta-analyses based on randomized controlled trials (RCTs) revealed convincingly that laparoscopic appendectomy (LA) which was initially performed by Semm [2] in 1983 and is widespread now has a tendency of replacing the open procedure as a standard treatment for AA with obvious advantages, including earlier bowel function recovery and postoperative oral intake, less invasiveness and postsurgical pain, shorter postoperative hospital stay, earlier return to normal diet, activities and work, lower rates of postoperative complications especially wound infection and mortality, and better cosmesis, despite possibly longer operation time, the difference of which between the two approaches is reducing [3].

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There are also evidences sustaining LA for children, obese population, and adults with complicated appendicitis [4]. However, a systematic review based on low-level evidences showed that LA might cause more fetal losses during pregnancy [5].

With the rapid progress of natural orifice translumenal endoscopic surgery, single-incision LA (SILA) emerged as an innovation, which allows minimally invasive surgery to be performed through a single incision, further reducing the trauma, and is gaining widespread acceptance because of its provision of a "scarless" abdominoplasty without increasing hazards [6]. Since the first SILA was conducted for AA by Pelosi [7] in 1992, there have been numerous trials comparing SILA with conventional three-port LA (TPLA). However, claims of reduced pain with improved cosmesis and faster recovery are unsubstantiatedly informed with weak and insufficient evidence [8]. Many other controversies remain, including surgical time, postoperative complications, and hospital duration [6].

Up till now, pooled comparisons [9–13] are mainly based on retrospective and nonrandomized observational trials with few available RCTs. None of them include studies published last year, when 5 novel RCTs with large samples emerged. Gao's [14] analysis also neglected the fact that St Peter' and Knott's results are based on the same population. Therefore, their unconvincing conclusions should be interpreted with caution due to considerable bias.

In this study, potential advantages of each technique were quantified using the meta-analytical method. Meta-analysis reaches the highest level of evidence when pooling data only from randomized trials [15], therefore our study which is carried out according to preferred reporting items for systematic reviews and meta-analysis (PRISMA) [16] guideline and based on intention to treat analysis systematically reviewing all the available high-quality RCTs comparing SILA with TPLA creates the highest level of evidence.

Materials and methods

Literature search

A systematic literature search with search terms "single/one-incision/port/site," "three-port," "conventional," "laparoscopic/laparoendoscopic," and "appendectomy/appendicectomy/appendicitis" and their combinations as key words was performed in MEDLINE, EMBASE, the Cochrane Library and Springer databases, and Google Scholar (Fig. 1). Special database functions like "related articles" and "explosion" were used to maximize our search, and cross-references, references from relevant articles and reviews were also screened. We also searched conference proceedings and ongoing trial databases. Language restrictions were not applied. The last search was performed on January 12th, 2014.

Inclusion criteria

Titles and abstracts of all identified articles were screened and we selected studies according to the following criteria: population-patients with AA (diagnosed as proposed by Katkhouda [17]) without age, gender, body mass index, and racial limitations; intervention and comparative intervention-clearly documented surgical technique of SILA versus TPLA with curative intent for AA including at least one of the five basic types, regardless of detailed equipment applied, and size and position of the port/incision; outcomes-at least one of the outcome measures reported below; study design-published and unpublished RCTs. If two studies from the same institution were identified, the most recent or the most informative was selected, unless they were reports from different periods or if the data of overlapping patients could be subtracted.

Exclusion criteria

Studies were excluded from our analysis if they did not meet the above inclusion criteria, or the study population included diseases other than AA (e.g., appendiceal carcinoid, chronic appendicitis) unless the data were presented separately, or it was impossible to extract or calculate appropriate data from the published results. Abstracts of RCTs were excluded as the surgical technique, methodological quality, and the risk of bias of these studies could not be assessed.

Types of interventions

Any appendectomy performed in the space generated by an insufflated pneumoperitoneum or by a wall lifting method, with visualization of the operative field mainly through a videolaparoscope was included. The technique was referred as SILA if all phases of the operation were performed initially through one incision regardless of incision size. As TPLA, we considered all procedures as "conventional" or "three-port" and performed initially through three abdominal ports. Techniques in which extra incisions or ports were used to facilitate the procedure half-way were not excluded.

Studies that included other types of resections (e.g., open appendectomy) or those that contained multivisceral resections were excluded unless the data were presented separatively.

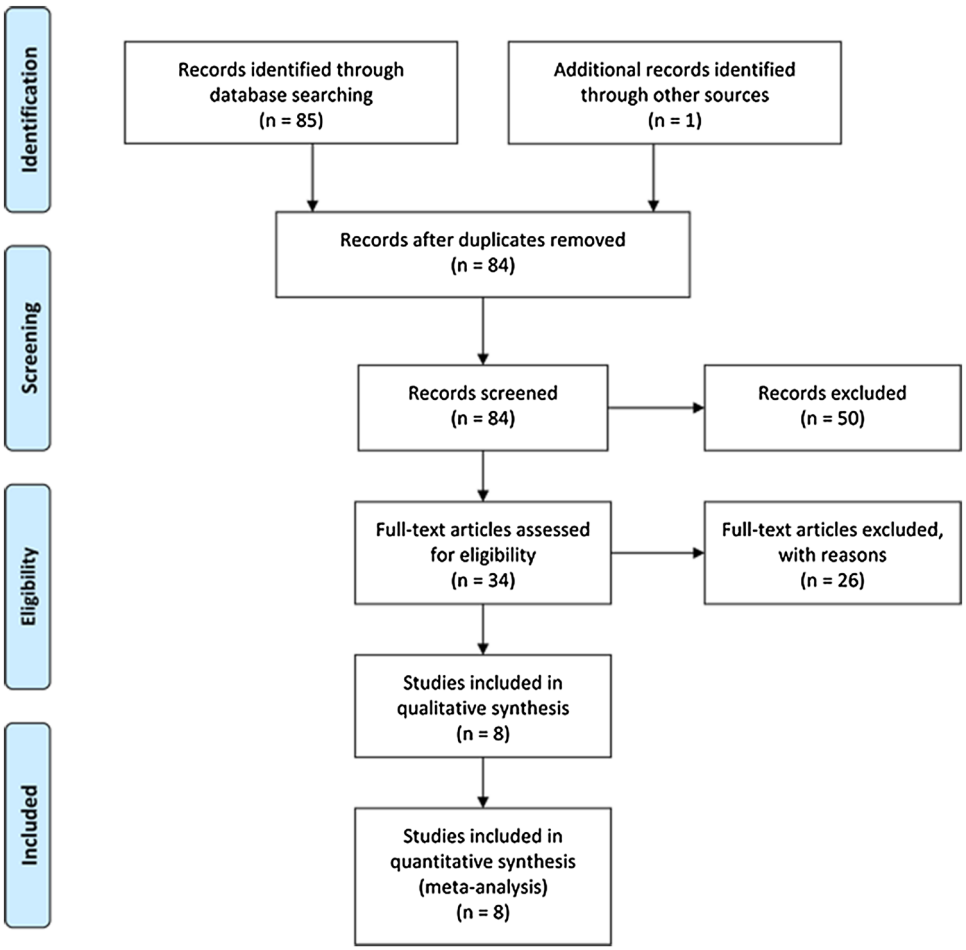


Fig. 1 PRISMA literature selection flow diagram. *PRISMA* preferred reporting items for systematic reviews and meta-analysis

Outcomes of interest and definitions

Primary outcomes were operating time (min), hospital duration (h), length of postsurgical hospital stay (h), days back to full activities, postsurgical complications, and reoperations. Secondary outcomes included extra trocars and drainages required, hours to regular diet, post-operational pain based on visual analog scale (VAS) [18], and application of analgesics. As described in the included trials, the operative time was recorded as the time from the first incision to the placement of the last suture in the skin. Patients were discharged after clinical examinations, body temperature, and leukocyte count were normal. Postsurgical duration was defined as the number of days in the hospital after the operation day. The days required for a return to work or normal activities were determined by patient follow-up assessment for at least 1 month. Postoperative complications were classified as medical (urinary events, nonsurgical infections, etc.) and surgical, which were further categorized as major (any fistula, any complication that required reoperation, all intra-abdominal collections, etc.) and minor (wound complications, bleeding events, ileus, etc). This classification system of major and minor surgical complications is based on Memorial Sloan-Kettering Cancer Center complication reporting system [19]. Patients' postoperative pain was scored using a VAS with scores ranging from 1 (absence of pain) to 10 (worst pain possible) [18], and number of patients who required analgesics post-appendectomy.

Data extraction

Titles and abstracts of all retrieved records, and subsequently full-text articles were examined independently by two authors (A.M.X. and L.H.) according to PRISMA [16] guideline. The following data were extracted separately by the same two authors for all included studies: reference of study, study population characteristics, study design, and inclusion and exclusion criteria. For dichotomous outcomes, the number of events was recorded and for continuous outcomes, means, and standard deviations (SDs) were registered. Population characteristics included number of participating subjects, the number and type of procedures performed, age, gender, body mass index, and

Table 1 Details of included RCTs comparing SILA with TPLA in our meta-analysis

Authors	Year, ethnicity	Period	Intention to treat analysis	Matched factors	Sample size
Park et al. [27]	2010, Korea	2009.4–2009.6	NR	1, 2, 5, 6	40
St. Peter et al. [28]	2011, America	2009.8–2010.10	Yes	1, 2, 3, 4, 5, 7	360
Teoh et al. [29]	2012, China	2009.10–2011.3	No	1, 2, 11	200
Frutos et al. [30]	2013, Spain	2009.9–2010.12	NR	1, 2, 3, 4, 11	184
Kye et al. [31]	2013, Korea	2009.2–2010.4	Yes	1, 4, 5, 6, 10	102
Lee et al. [32]	2013, Korea	2010.3–2011.9	No	1, 2, 4, 5, 6, 13	248
Perez et al. [33]	2013, America	2009.6–2011.1	NR	1, 2, 3, 11, 12	50
Sozutek et al. [34]	2013, Turkey	2010.9–2011.5	NR	1, 2, 4, 8, 9	50

RCTs randomized controlled trials, *SILA* single-incision laparoscopic appendectomy, *TPLA* three-port laparoscopic appendectomy, *NR* not reported, *1* age, *2* gender, *3* weight, *4* body mass index, *5* initial leucocyte count, *6* initial C-reactive protein, *7* admission temperature, *8* American Society of Anesthesiologists (ASA) score, *9* previous abdominal surgery, *10* duration of symptoms, *11* appendicitis type, *12* race, *13* erythrocyte sedimentation rate (ESR)

Table 2 Patients' characteristics

Authors	Method	*n*	Age (year)	Sex (M/F)	Weight (kg)	BMI (kg/m^2)	CRP (mg/L)	WBC (10^9/L)
Park et al. [27]	SILA	20	25.0	9/11	NR	NR	38.0	11.6
	TPLA	20	27.2	8/12	NR	NR	38.6	12.1
St. Peter et al. [28]	SILA	180	11.1 ± 3.5	99/81	42.7 ± 18.5	19.4 ± 4.9	NR	14.6 ± 5.4
	TPLA	180	11.1 ± 3.3	99/81	42.5 ± 17.4	19.6 ± 4.5	NR	14.6 ± 5.2
Teoh et al. [29]	SILA	100	39.19 ± 15.55	58/40	NR	NR	NR	NR
	TPLA	100	40.65 ± 15.68	59/38	NR	NR	NR	NR
Frutos et al. [30]	SILA	91	28.04 ± 11.03	42/49	67.27 ± 14.38	23.84 ± 3.98	NR	NR
	TPLA	93	31.02 ± 12.41	47/46	68.13 ± 13.84	24.02 ± 3.84	NR	NR
Kye et al. [31]	SILA	51	27.55 ± 12.40	NR	NR	22.03 ± 4.07	722.4 ± 670.8	11.26 ± 3.89
	TPLA	51	29.20 ± 13.98	NR	NR	21.97 ± 3.49	374.8 ± 566.5	12.93 ± 4.05
Lee et al. [32]	SILA	124	28.4 ± 15.4	64/52	NR	21.4 ± 3.2	3.5 ± 4.8	12.04 ± 3.89
	TPLA	124	28.5 ± 17.2	68/45	NR	22.7 ± 4.4	2.5 ± 3.3	12.67 ± 4.55
Perez et al. [33]	SILA	25	8.7 ± 0.6	10/15	36.25 (14.5–80.3)	NR	NR	NR
	TPLA	25	8.9 ± 0.6	15/10	35.17 (12–101)	NR	NR	NR
Sozutek et al. [34]	SILA	25	30.6 ± 12.4	12/13	NR	23.2 ± 3.79	NR	NR
	TPLA	25	30.0 ± 11.0	7/18	NR	23.1 ± 2.58	NR	NR

All values are n or mean ± SD or mean (range)

M male, *F* female, *BMI* body mass index, *CRP* C-reactive protein, *WBC* white blood count on admission, *SILA* single-incision laparoscopic appendectomy, *TPLA* three-port laparoscopic appendectomy, *NR* not reported

pathological type of AA. In case of discrepancies, a third author (T.J.L.) was consulted and agreement was reached by consensus.

Missing data were handled by the following methods. Missing SDs were imputed on the basis of ranges when available [20]. If both means and SDs were missing, they were imputed on the basis of the medians and ranges or on the basis of medians and interquartile ranges, according to availability [20]. If neither a range nor any other measure of dispersion was available, then the study data were not applied in meta-analysis.

Risk of bias assessment

Risk of bias was assessed for all articles by individual components using both the Cochrane Collaboration's tool for assessing risk of bias and the Jadad scoring system [21].

Statistical analysis

This study was carried out in line with the recommendations of the PRISMA [16] statement. Statistical analyses were performed following the recommendations of the

Cochrane Collaboration Guidelines [22]. Outcomes reported by 2 or more studies were pooled in meta-analyses. Our study was based on intention to treat analysis.

Dichotomous and continuous outcomes were presented as risk ratios (RRs), rate differences (RDs), and weighted mean differences (WMDs), respectively. Data were pooled using the Mantel–Haenszel and the inverse-variance method for dichotomous and continuous outcomes, respectively. Trials with zero events in both arms were excluded from meta-analysis. Trials with zero events in 1 arm were included in the analysis by adding a continuity correction of 0.5 to all cells in the 2 × 2 table of that study. As a robustness assessment, meta-analyses with RCTs with 0 event in 1 arm were also performed using risk differences in a sensitivity analysis. For all analyses, the 95 % confidence interval (CI) was calculated. Heterogeneity was calculated using Higgins χ^2 test, and inconsistency in study effects was quantified by I^2 values [23]. The fixed-effects model was used if no heterogeneity was present (χ^2 $P > 0.100$ and $I^2 < 50$ %). If excessive heterogeneity was present, data were first rechecked and the DerSimonian random-effects model was used when heterogeneity persisted [24]. Funnel plots were used to help identify the presence of publication or other types of bias. Subgroup analysis was planned for studies with and without perforated AA, and pregnacy, and total cases more and less than 150 (cut-off value set in line with the median of the sample size of enrolled RCTs) after the overall analysis. Review Manager software (RevMan© v. 5.0) provided by the Cochrane Collaboration was used for data management and statistical analyses.

Results

Selected RCTs characteristics

A total of 86 potential relevant publications were identified (Fig. 1). We then identified 34 full-text articles comparing SILA with TPLA and found 24 studies did not randomly allocate patients. One RCT [25] comparing the two methods has been registered, but without any accessible data.

Table 3 Inclusion criteria for LA eligibility and indication for AA requiring surgical treatment

Authors	Symptoms and/or signs	Preoperative US/CT signs	Laboratory studies	Severe comorbidities	Previous abdominal surgery
Park et al. [27]	Yes	Yes	Yes	No	No
St. Peter et al. [28]	NR	NR	Yes	NR	NR
Teoh et al. [29]	Yes	No	Yes	No	No
Frutos et al. [30]	Yes	Yes	NR	No	NR
Kye et al. [31]	NR	NR	Yes	NR	NR
Lee et al. [32]	Yes	Yes	Yes	No	NR
Perez et al. [33]	Yes	NR	NR	NR	NR
Sozutek et al. [34]	Yes	Yes	Yes	NR	Yes

LA laparoscopic appendectomy, *AA* acute appendicitis, *US* ultrasound, *CT* computed tomography, *NR* not reported

Table 4 Distribution of patients according to histopathologic type of appendicitis

Authors	Exudative appendicitis		Suppurative appendicitis		Perforated appendicitis		Gangrenous appendicitis		Periappendiceal abscess	
	SILA	TPLA	SILA	TPLA	SILA	TPLA	SILA	TPLA	SILA	TPLA
Park et al. [27]	NR	NR	NR	NR	0	0	NR	NR	0	0
St. Peter et al. [28]	NR	NR	NR	NR	0	0	NR	NR	NR	NR
Teoh et al. [29]	NR	NR	NR	NR	15	15	19	18	8	12
Frutos et al. [30]	10	16	67	65	0	0	14	12	0	0
Kye et al. [31]	NR	NR	NR	NR	9	7	NR	NR	NR	NR
Lee et al. [32]	45	49	43	38	0	0	0	2	18	26
Perez et al. [33]	NR	NR	NR	NR	5	3	NR	NR	NR	NR
Sozutek et al. [34]	15	15	6	4	4	6	0	0	1	0

SILA single-incision laparoscopic appendectomy, *TPLA* three-port laparoscopic appendectomy, *NR* not reported

Table 5 Quality assessment and risk of bias summary

	Park et al. [27]	St. Peter et al. [28]	Teoh et al. [29]	Frutos et al. [30]	Kye et al. [31]	Lee et al. [32]	Perez et al. [33]	Sozutek et al. [34]
Adequate sequence generation?	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Allocation concealment?	Unclear	Yes	Yes	Yes	Unclear	Unclear	Unclear	Unclear
Blinding (observer)?	Unclear	Yes	Yes	Yes	Unclear	Unclear	Unclear	Unclear
Blinding (patient)?	Unclear	Yes	Yes	Unclear	Unclear	Unclear	Unclear	Unclear
Incomplete outcome data addressed?	No	Yes	Yes	Yes	No	Unclear	No	No
Postoperative protocol reported?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Adequate report on loss to follow-up?	Unclear	No	Yes	Unclear	Unclear	Unclear	Unclear	Unclear
Free of selective reporting?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Free of other bias?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Sample size calculation?	No	Yes	Yes	Yes	Yes	Yes	Yes	No
Jadad score	1	5	5	3	2	4	3	2

One RCT [26] was excluded for duplicate publication based on the same population with St. Peter's. Finally, eight original RCTs [27–34] comparing SILA with TPLA when treating AA which met the eligibility criteria were identified. Among them 4 publications excluded patients suffering from perforated AA, while the other 4 articles set no special limitations on type of AA.

The 8 included RCTs were published between 2010 and 2013, and conducted between February 2009 and November 2011 with 1 week to 35 months of follow-up. A total of 1234 patients were included in our analysis with 616 undergoing SILA (49.9 %) and 618 (50.1 %) undergoing TPLA (Table 1). LA was performed in all patients, with either 1 incision or 3 ports in abdomen. Patients' characteristics are listed in Table 2. All patients had proof of AA on symptoms and/or signs and/or preoperative ultrasound/computed tomography and/or laboratory studies (Table 3). Regarding the preoperative clinical criteria used to select patients, four trials included patients with perforated AA for the laparoscopic technique, and these patients showed no difference of characteristics between both arms (Table 4). In total, 1,170 patients (94.8 %) were imperforated. Overall, there were only 2 conversions to OA (0.16 %), related to incomplete repair of appendiceal base during SILA and an identified mass-forming lesion during TPLA, respectively. Matching of demographic factors was almost complete and all studies were adequately matched in all the factors reviewed (Table 1). Before LA, the two groups did not differ significantly in terms of age ($Z = 1.29$, $P = 0.20$), gender ($Z = 0.20$, $P = 0.84$), weight ($Z = 0.15$, $P = 0.88$), body mass index ($Z = 1.74$, $P = 0.08$), inflammatory parameters [C-reactive protein ($Z = 0.22$, $P = 0.83$) and leukocyte count ($Z = 1.72$, $P = 0.09$)], or type of appendicitis [exudative appendicitis ($Z = 1.01$, $P = 0.31$), suppurative appendicitis ($Z = 1.07$, $P = 0.28$), perforated appendicitis ($Z = 0.27$, $P = 0.79$), gangrenous appendicitis ($Z = 0.17$, $P = 0.86$), and periappendiceal abscess ($Z = 1.46$, $P = 0.15$)] (Tables 2, 4).

Methodological quality assessment

The trials had relatively good methodological quality with a mean Jadad score of 3.125 (range 1–5). However, they mostly suffered from methodologic drawbacks frequently seen in surgical RCTs in general, mainly difficulties in concealing the allocation of patients, the inherent complexity of blinding between two techniques, and small number of patients included in part of the researches. Five trials did not report double blinding and allocation concealment and one did not report loss to follow-up. Six trials reported a sample size calculation. Seven trials had adequate sequence generation (Table 5)

Primary outcomes

Detailed data and analyses by categories are available in Tables 6 and 7.

Operative time

Results were available for all RCTs. There existed significant heterogeneity ($\chi^2 = 39.76$, $P < 0.00001$, $I^2 = 82$ %) between two groups, so a randomized-effect model was chosen. Operative time was approximately 5 min longer in the SILA group than in the TPLA group (43 vs 38; WMD: 5.96; 95 % CI 2.54–9.38; $P = 0.0006$; Fig. 2A). However, two reports [31, 33] comparing 2 techniques dealing with perforated AA separately revealed no significant difference between 2 procedures (46 vs 49; WMD: 4.15; 95 % CI −15.58 to 23.89; $P = 0.68$), based on a randomized-effect model due to significant heterogeneity ($\chi^2 = 2.85$, $P = 0.09$, $I^2 = 65$ %).

Table 6 Primary outcomes

Authors	Method	Operating time (min)	Hospital stay (h)	Postsurgical stay (h)	Days to full activities	Reoperation
Park et al. [27]	SILA	63.5 ± 13.2	NR	86.4	NR	NR
	TPLA	54.0 ± 12.5	NR	93.6	NR	NR
St. Peter et al. [28]	SILA	35.2 ± 14.5	NR	22.7 ± 6.2	7.5 ± 5.8	NR
	TPLA	29.8 ± 11.6	NR	22.2 ± 6.8	8.5 ± 6.2	NR
Teoh et al. [29]	SILA	63.0 ± 27.2	84.72 ± 70.08	NR	6.17 ± 4.21	NR
	TPLA	60.2 ± 31.7	76.80 ± 56.64	NR	6.38 ± 4.10	NR
Frutos et al. [30]	SILA	38.13 ± 13.49	18.86 ± 9.77	NR	NR	0
	TPLA	32.12 ± 12.44	21.32 ± 11.72	NR	NR	1
Kye et al. [31]	SILA	37.00 ± 15.46	NR	66.72 ± 29.28	3.22 ± 1.04	NR
	TPLA	38.45 ± 15.26	NR	67.92 ± 30.96	3.94 ± 1.43	NR
Lee et al. [32]	SILA	43.8 ± 21.3	72 (48–96)	NR	NR	0
	TPLA	35.8 ± 18.9	72 (48–120)	NR	NR	1
Perez et al. [33]	SILA	46.8 ± 3.7	40.3	NR	NR	NR
	TPLA	34.8 ± 2.5	36.7	NR	NR	NR
Sozutek et al. [34]	SILA	32.6 ± 9.9	26.4 ± 7.2	NR	NR	0
	TPLA	29.5 ± 6.8	28.8 ± 19.2	NR	NR	0

Authors	Method	Overall complications	Major surgical complications	Minor surgical complications	Medical complications	Ileus	Abdominal infections	Wound infections
Park et al. [27]	SILA	2	1	1	0	0	1	1
	TPLA	2	0	2	0	1	0	1
St. Peter et al. [28]	SILA	6	0	6	0	NR	0	6
	TPLA	4	1	3	0	NR	1	3
Teoh et al. [29]	SILA	15	4	10	1	2	NR	8
	TPLA	15	3	9	3	4	NR	5
Frutos et al. [30]	SILA	5	0	4	1	NR	NR	NR
	TPLA	4	0	3	1	NR	NR	NR
Kye et al. [31]	SILA	3	2	1	0	1	1	0
	TPLA	3	2	1	0	0	1	1
Lee et al. [32]	SILA	17	6	9	2	1	6	6
	TPLA	20	3	15	2	1	2	12
Perez et al. [33]	SILA	1	0	1	0	0	0	0
	TPLA	0	0	0	0	0	0	0
Sozutek et al. [34]	SILA	1	0	1	0	0	NR	1
	TPLA	1	0	1	0	0	NR	1

SILA single-incision laparoscopic appendectomy, *TPLA* three-port laparoscopic appendectomy, *NR* not reported, *VAS* visual analog scale

Hospital and postsurgical duration

There being no significant heterogeneity or bias (Fig. 4A), fixed-effect model chosen showed no significant difference in either overall (4 RCTs, 58 vs 59; WMD −0.96; 95 % CI −2.86 to 0.94; $P = 0.32$; Fig. 2B) or post-LA hospital stay (2 RCTs, 32 vs 32; WMD: 0.48; 95 % CI −0.86 to 1.81; $P = 0.48$) between 2 procedures.

Return to normal activities

Follow-ups provided by 3 trials supported that SILA group had a significantly earlier return to full activities (6 vs 7; WMD: −0.68; 95 % CI −1.10 to −0.26; $P = 0.001$; Fig. 2C), without significant heterogeneity, but St. Peter [28] found no significant difference in days to return to school among children patients. Teoh [29] further reported no significant difference in quality-of-life in short-term.

Postoperative complications

The included trials reported no mortality. There were no significant heterogeneities or biases demonstrated by funnel plots for all parameters (Fig. 4B–D), so fixed-effect models were applied. The combined data from all trials showed that the overall (8 vs 8 %; RR: 1.02; 95 % CI 0.71–1.48; $P = 0.91$; Fig. 2D), surgical [major (2 vs 1 %; RR: 1.40; 95 % CI 0.63–3.11; $P = 0.41$; Fig. 2E) and minor (5 vs 6 %; RR: 0.97; 95 % CI 0.62–1.54; $P = 0.91$; Fig. 2F)], and medical (1 vs 1 %; RR: 0.67; 95 % CI 0.19–2.35; $P = 0.53$, Fig. 2G) complications were all comparable between 2 groups.

Through a subcategory analysis of postoperative complications, we found that rates of ileus (6 RCTs; 1 vs 2 %; RR: 0.71; 95 % CI 0.23–2.22; $P = 0.56$; Fig. 2H), abdominal (5 RCTs; 2 vs 1 %; RR: 1.80; 95 % CI 0.61–5.31; $P = 0.29$; Fig. 2I), and wound (7 RCTs; 4 vs 4 %; RR: 0.96; 95 % CI 0.55–1.68; $P = 0.88$; Fig. 2J) infections were all similar in both groups, all based on fixed-effect model thanks to insignificant heterogeneity or bias (Fig. 4E–G). Reoperation rates were also comparable (3 RCTs [30, 32, 34]; 0 vs 1 %; RR: 0.34; 95 % CI 0.04–3.21; $P = 0.34$) for both procedures.

Secondary outcomes

Detailed data and analyses by categories are available in Tables 8 and 9.

Extra trocars and drainages

More extra trocars were observed among patients undergoing SILA (6 RCTs; 7 vs 0 %; RR: 12.36; 95 % CI 3.83–39.90; $P < 0.0001$; Fig. 3A) based on a fixed-effect model due to insignificant heterogeneity and bias (Fig. 4H), and RD was also calculated with a significant difference found (RD: 0.05; 95 % CI 0.01–0.10; $P = 0.03$; Fig. 3B) using a randomized-effect model due to significant heterogeneity ($\chi^2 = 21.28$, $P = 0.0007$, $I^2 = 77$ %), while drainages needed revealed by 3 studies were comparable (8 vs 11 %; RR: 0.77; 95 % CI 0.45–1.33; $P = 0.35$; Fig. 3C).

Fig. 2 **A** Operative time by SILA and TPLA techniques, showing SILA takes longer to complete. **B** Hospital duration by SILA and TPLA techniques, showing no difference. **C** Days needed to return to full activities, showing patients undergoing SILA recovers faster. **D** Overall complications, **E** major surgical complications, **F** minor surgical complications, **G** medical complications, **H** ileus, **I** abdominal infections, and **J** wound infections, all showing similar results between SILA and TPLA procedures. *SILA* single-incision laparoscopic appendectomy, *TPLA* three-port laparoscopic appendectomy

Postoperative pain

Significant heterogeneities were observed for VAS scores 12 ($\chi^2 = 8.21$, $P = 0.004$, $I^2 = 88$ %) and 24 h ($\chi^2 = 3.14$, $P = 0.08$, $I^2 = 68$ %) post-LA, so randomized-effect models were used. Results revealed that there were no significant differences in both scores (2 RCTs; 3 vs 3; WMD: −0.51; 95 % CI −1.51 to 0.49; $P = 0.32$ and 2 RCTs; 3 vs 3; WMD: −0.34; 95 % CI −1.01 to 0.32; $P = 0.31$). This was accompanied by a comparable prevalence of analgesics use (2 RCTs; 75 vs 88 %; RR: 0.89; 95 % CI 0.76–1.05; $P = 0.16$). St. Peter [28] also reported similar results as to days and doses of prescribed analgesics after hospital discharge. However, Teoh [29] revealed

Table 7 Analysis of major outcomes by categories

Category	No. RCTs	SILA	TPLA	RR	WMD	95 % CI	*P*
Operative time (min)	8	43 ($n = 616$)	38 ($n = 618$)		5.96	2.54 to 9.38	0.0006
Hospital duration (h)	4	58 ($n = 340$)	59 ($n = 342$)		−0.96	−2.86 to 0.94	0.32
Postsurgical stay (h)	2	32 ($n = 231$)	32 ($n = 231$)		0.48	−0.86 to 1.81	0.48
Days to full activities	3	6 ($n = 331$)	7 ($n = 331$)		−0.68	−1.10 to −0.26	0.001
Overall complications	8	50/616 (8 %)	49/618 (8 %)	1.02		0.71–1.48	0.91
Major surgical complications	8	13/616 (2 %)	9/618 (1 %)	1.40		0.63–3.11	0.41
Minor surgical complications	8	33/616 (5 %)	34/618 (6 %)	0.97		0.62–1.54	0.91
Medical complications	8	4/616 (1 %)	6/618 (1 %)	0.67		0.19–2.35	0.53
Ileus	6	4/345 (1 %)	6/345 (2 %)	0.71		0.23–2.22	0.56
Abdominal infections	5	8/400 (2 %)	4/400 (1 %)	1.80		0.61–5.31	0.29
Wound infections	7	22/525 (4 %)	23/525 (4 %)	0.96		0.55–1.68	0.88
Reoperations	3	0/240 (0 %)	2/242 (1 %)	0.34		0.04–3.21	0.34

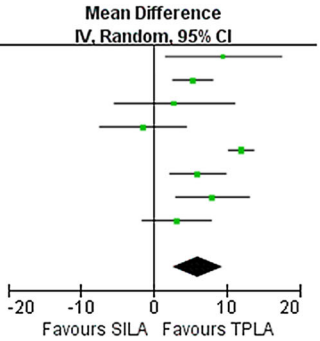
Relative risks less than one favor the sila approach

RCTs randomized controlled trials, *SILA* single-incision laparoscopic appendectomy, *TPLA* three-port laparoscopic appendectomy, *RR* risk ratio, *WMD* weighted mean difference, *CI* confidence interval

A

Study or Subgroup	SILA Mean	SILA SD	SILA Total	TPLA Mean	TPLA SD	TPLA Total	Weight	Mean Difference IV, Random, 95% CI	Year
Park 2010	63.5	13.2	20	54	12.5	20	8.9%	9.50 [1.53, 17.47]	2010
St. Peter 2011	35.2	14.5	180	29.8	11.6	180	15.4%	5.40 [2.69, 8.11]	2011
Teoh 2012	63	27.2	100	60.2	31.7	100	8.6%	2.80 [-5.39, 10.99]	2012
Kye 2013	37	15.46	51	38.45	15.26	51	11.2%	-1.45 [-7.41, 4.51]	2013
Perez 2013	46.8	3.7	25	34.8	2.5	25	16.3%	12.00 [10.25, 13.75]	2013
Frutos 2013	38.13	13.49	91	32.12	12.44	93	14.2%	6.01 [2.26, 9.76]	2013
Lee 2013	43.8	21.3	124	35.8	18.9	124	12.5%	8.00 [2.99, 13.01]	2013
Sozutek 2013	32.6	9.9	25	29.5	6.8	25	12.9%	3.10 [-1.61, 7.81]	2013
Total (95% CI)			**616**			**618**	**100.0%**	**5.96 [2.54, 9.38]**	

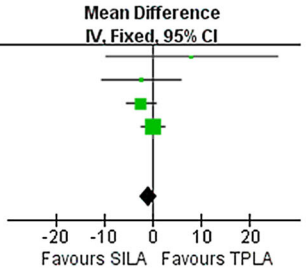
Heterogeneity: Tau² = 17.85; Chi² = 39.76, df = 7 (P < 0.00001); I² = 82%
Test for overall effect: Z = 3.42 (P = 0.0006)



B

Study or Subgroup	SILA Mean	SILA SD	SILA Total	TPLA Mean	TPLA SD	TPLA Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
Teoh 2012	84.72	70.08	100	76.8	56.64	100	1.2%	7.92 [-9.74, 25.58]	2012
Sozutek 2013	26.4	7.2	25	28.8	19.2	25	5.6%	-2.40 [-10.44, 5.64]	2013
Frutos 2013	18.86	9.77	91	21.32	11.72	93	37.2%	-2.46 [-5.57, 0.65]	2013
Lee 2013	72	8	124	72	12	124	56.0%	0.00 [-2.54, 2.54]	2013
Perez 2013	40.3	0	25	36.7	0	25		Not estimable	2013
Total (95% CI)			**365**			**367**	**100.0%**	**-0.96 [-2.86, 0.94]**	

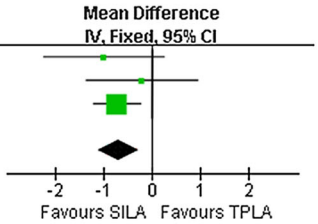
Heterogeneity: Chi² = 2.53, df = 3 (P = 0.47); I² = 0%
Test for overall effect: Z = 0.99 (P = 0.32)



C

Study or Subgroup	SILA Mean	SILA SD	SILA Total	TPLA Mean	TPLA SD	TPLA Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
St. Peter 2011	7.5	5.8	180	8.5	6.2	180	11.5%	-1.00 [-2.24, 0.24]	2011
Teoh 2012	6.17	4.21	100	6.38	4.1	100	13.3%	-0.21 [-1.36, 0.94]	2012
Kye 2013	3.22	1.04	51	3.94	1.43	51	75.2%	-0.72 [-1.21, -0.23]	2013
Total (95% CI)			**331**			**331**	**100.0%**	**-0.68 [-1.10, -0.26]**	

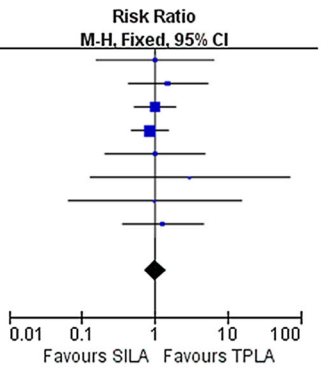
Heterogeneity: Chi² = 0.92, df = 2 (P = 0.63); I² = 0%
Test for overall effect: Z = 3.19 (P = 0.001)



D

Study or Subgroup	SILA Events	SILA Total	TPLA Events	TPLA Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Park 2010	2	20	2	20	4.0%	1.00 [0.16, 6.42]	2010
St. Peter 2011	6	180	4	180	8.1%	1.50 [0.43, 5.23]	2011
Teoh 2012	15	100	15	100	30.3%	1.00 [0.52, 1.93]	2012
Lee 2013	17	124	20	124	40.4%	0.85 [0.47, 1.54]	2013
Kye 2013	3	51	3	51	6.1%	1.00 [0.21, 4.72]	2013
Perez 2013	1	25	0	25	1.0%	3.00 [0.13, 70.30]	2013
Sozutek 2013	1	25	1	25	2.0%	1.00 [0.07, 15.12]	2013
Frutos 2013	5	91	4	93	8.0%	1.28 [0.35, 4.61]	2013
Total (95% CI)		**616**		**618**	**100.0%**	**1.02 [0.71, 1.48]**	
Total events	50		49				

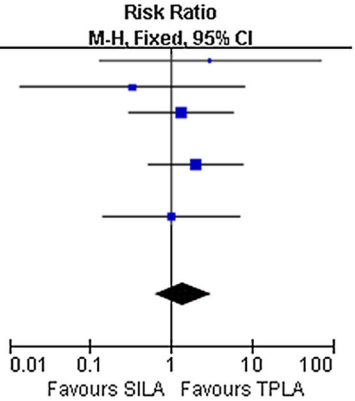
Heterogeneity: Chi² = 1.30, df = 7 (P = 0.99); I² = 0%
Test for overall effect: Z = 0.12 (P = 0.91)

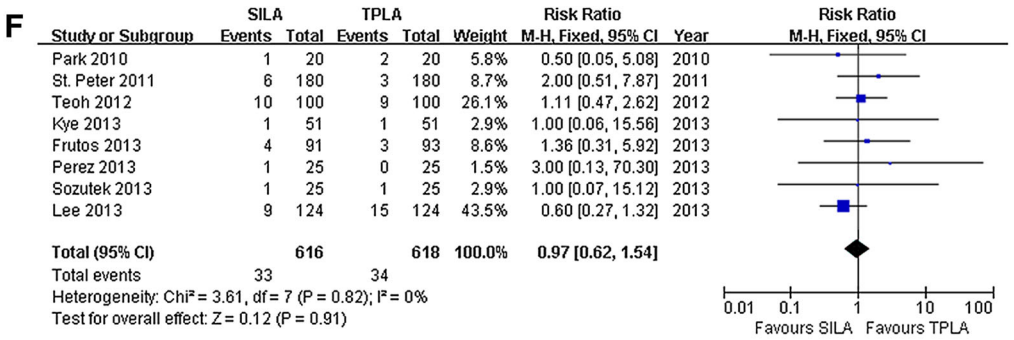


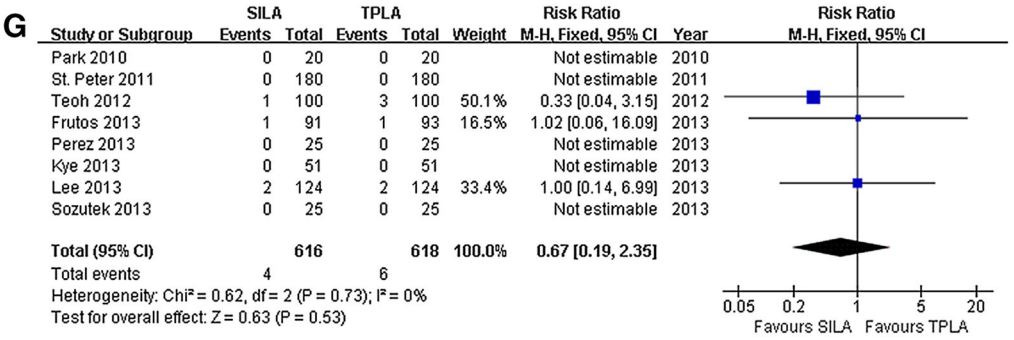
E

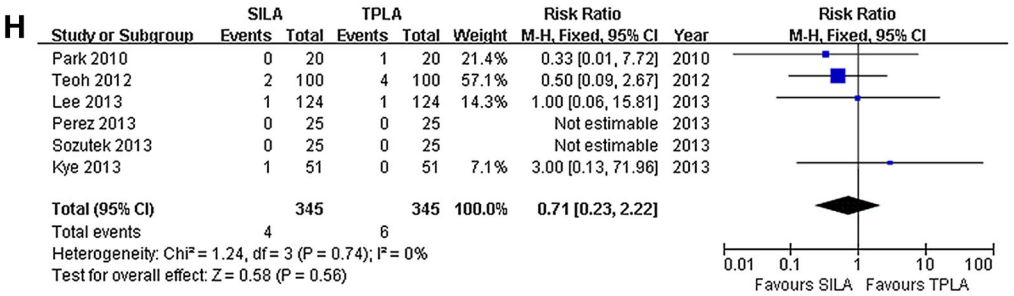
Study or Subgroup	SILA Events	SILA Total	TPLA Events	TPLA Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Park 2010	1	20	0	20	5.0%	3.00 [0.13, 69.52]	2010
St. Peter 2011	0	180	1	180	15.0%	0.33 [0.01, 8.13]	2011
Teoh 2012	4	100	3	100	30.0%	1.33 [0.31, 5.81]	2012
Perez 2013	0	25	0	25		Not estimable	2013
Lee 2013	6	124	3	124	30.0%	2.00 [0.51, 7.82]	2013
Frutos 2013	0	91	0	93		Not estimable	2013
Kye 2013	2	51	2	51	20.0%	1.00 [0.15, 6.83]	2013
Sozutek 2013	0	25	0	25		Not estimable	2013
Total (95% CI)		**616**		**618**	**100.0%**	**1.40 [0.63, 3.11]**	
Total events	13		9				

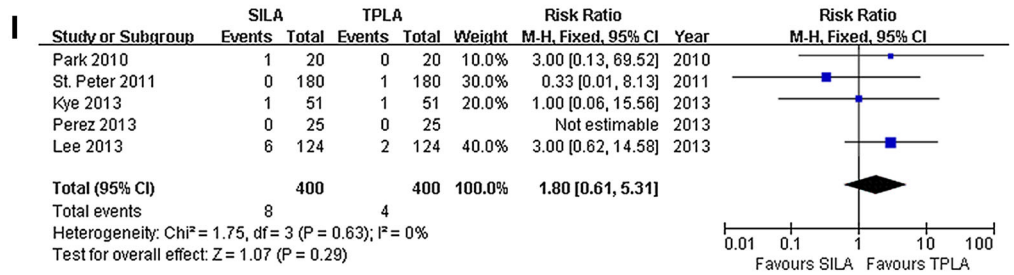
Heterogeneity: Chi² = 1.39, df = 4 (P = 0.85); I² = 0%
Test for overall effect: Z = 0.83 (P = 0.41)











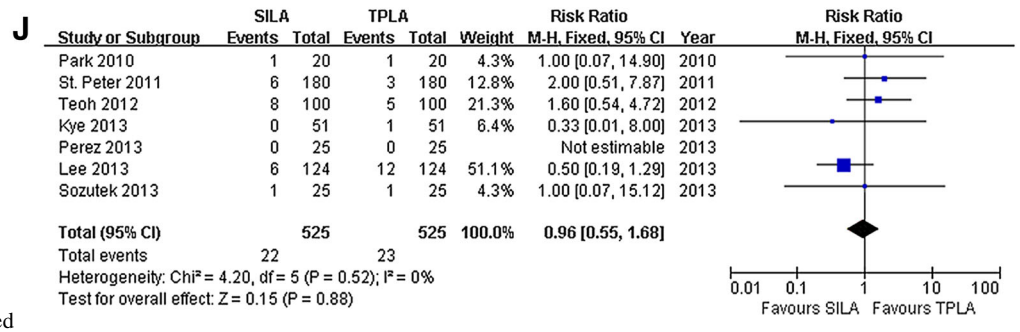


Fig. 2 continued

Table 8 Secondary outcomes

Authors	Method	Extra trocars	Drainages	Hours to regular diet	VAS score (12 h)	VAS score (24 h)	Analgesics requirements
Park et al. [27]	SILA	1	1	NR	6.6	5	NR
	TPLA	0	0	NR	4.2	3.5	NR
St. Peter et al. [28]	SILA	18	NR	7.2 ± 5.1	NR	NR	NR
	TPLA	0	NR	6.9 ± 5.2	NR	NR	NR
Teoh et al. [29]	SILA	NR	14	52.8 ± 24.96	5.7	5.5	NR
	TPLA	NR	18	71.76 ± 127.44	5.4	5.0	NR
Frutos et al. [30]	SILA	1	NR	NR	2.76 ± 1.64	NR	NR
	TPLA	0	NR	NR	3.78 ± 1.76	NR	NR
Kye et al. [31]	SILA	1	NR	NR	NR	3.22 ± 1.22	38
	TPLA	0	NR	NR	NR	3.90 ± 1.46	41
Lee et al. [32]	SILA	12	5	NR	2.81	1.88	NR
	TPLA	0	8	NR	2.91	2.06	NR
Perez et al. [33]	SILA	NR	NR	NR	NR	NR	NR
	TPLA	NR	NR	NR	NR	NR	NR
Sozutek et al. [34]	SILA	1	NR	6.3 ± 0.6	2.1 ± 0.97	2.0 ± 0.95	19
	TPLA	0	NR	6.3 ± 0.6	2.1 ± 0.81	2.0 ± 1.00	23

SILA single-incision laparoscopic appendectomy, *TPLA* three-port laparoscopic appendectomy, *VAS* visual analog scale, *NR* not reported

Table 9 Analysis of secondary outcomes by categories

Category	No. RCTs	SILA	TPLA	RR	WMD	95 % CI	*P*
Extra trocars	6	34/491 (7 %)	0/493 (0 %)	12.36		3.83–39.9	<0.0001
Drainages	3	20/244 (8 %)	26/244 (11 %)	0.77		0.45–1.33	0.35
Time to regular diet (h)	3	22 ($n = 305$)	28 ($n = 305$)		0.02	−0.29 to 0.34	0.88
VAS 12 h post-surgery	2	3 ($n = 116$)	3 ($n = 118$)		−0.51	−1.51 to 0.49	0.32
VAS 24 h post-surgery	2	3 ($n = 76$)	3 ($n = 76$)		−0.34	−1.01 to 0.32	0.31
Analgesics requirement	2	57/76 (75 %)	64/76 (88 %)	0.89		0.76–1.05	0.16

Relative risks less than one favor the sila approach

RCTs randomized controlled trials, *SILA* single-incision laparoscopic appendectomy, *TPLA* three-port laparoscopic appendectomy, *RR* risk ratio, *WMD* weighted mean difference, *CI* confidence interval

more severe pain experienced by patients undergoing SILA upon coughing or standing, but with similar pain score at rest.

Time when regular diet began

There existing no significant heterogeneity, a fixed-effect model was applied. No significant discrepancy was found in time to regular diet between 2 approaches (3 RCTs; 22 vs 28; WMD: 0.02; 95 % CI −0.29 to 0.34; $P = 0.88$; Fig. 3D).

Sensitivity tests

Kye's data ignored, patients undergoing 2 procedures returned to normal activity after comparable period of time (7 vs 8; WMD: −0.58; 95 % CI −1.42 to 0.27; $P = 0.18$; Fig. 5A). Either St. Peter's (5 vs 0 %; RD: 0.04; 95 % CI −0.01 to 0.09; $P = 0.08$; Fig. 5B) or Lee's (6 vs 0 %; RD: 0.04; 95 % CI −0.01 to 0.09; $P = 0.10$; Fig. 5C) study being excluded, extra trocars applied in 2 procedures were comparable when RD was calculated. Sensitivity analyses of all the other primary and secondary outcomes with 0 event in 1 arm yielded similar results. Funnel plots (Fig. 4) and an exhaustive literature search conferred a substantial degree of confidence in our pooled findings.

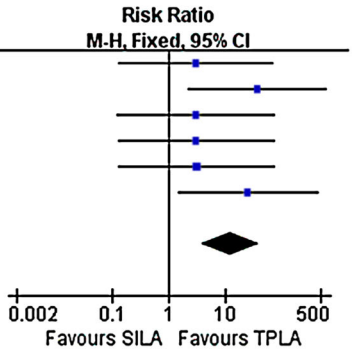
Subgroup analysis

We divided subgroups according to whether pregnancy or perforation was included and by using a 150 cases cut-point (Table 10). We found differences of surgical duration

A

Study or Subgroup	SILA Events	SILA Total	TPLA Events	TPLA Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Park 2010	1	20	0	20	16.7%	3.00 [0.13, 69.52]	2010
St. Peter 2011	18	180	0	180	16.7%	37.00 [2.25, 609.33]	2011
Kye 2013	1	51	0	51	16.7%	3.00 [0.13, 71.96]	2013
Sozutek 2013	1	25	0	25	16.7%	3.00 [0.13, 70.30]	2013
Frutos 2013	1	91	0	93	16.5%	3.07 [0.13, 74.28]	2013
Lee 2013	12	124	0	124	16.7%	25.00 [1.50, 417.67]	2013
Total (95% CI)		**491**		**493**	**100.0%**	**12.36 [3.83, 39.90]**	
Total events	34		0				

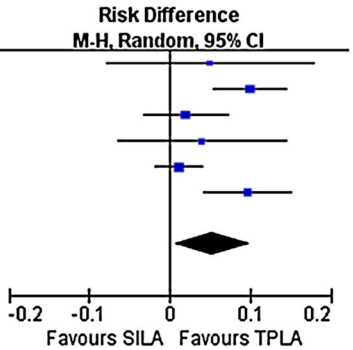
Heterogeneity: Chi² = 3.88, df = 5 (P = 0.57); I² = 0%
Test for overall effect: Z = 4.21 (P < 0.0001)



B

Study or Subgroup	SILA Events	SILA Total	TPLA Events	TPLA Total	Weight	Risk Difference M-H, Random, 95% CI	Year
Park 2010	1	20	0	20	8.8%	0.05 [-0.08, 0.18]	2010
St. Peter 2011	18	180	0	180	20.1%	0.10 [0.06, 0.14]	2011
Kye 2013	1	51	0	51	18.8%	0.02 [-0.03, 0.07]	2013
Sozutek 2013	1	25	0	25	11.3%	0.04 [-0.06, 0.14]	2013
Frutos 2013	1	91	0	93	22.3%	0.01 [-0.02, 0.04]	2013
Lee 2013	12	124	0	124	18.6%	0.10 [0.04, 0.15]	2013
Total (95% CI)		**491**		**493**	**100.0%**	**0.05 [0.01, 0.10]**	
Total events	34		0				

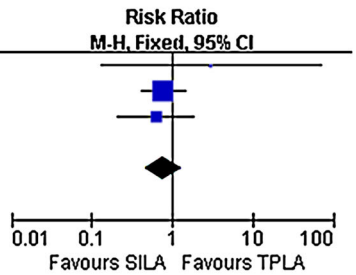
Heterogeneity: Tau² = 0.00; Chi² = 21.28, df = 5 (P = 0.0007); I² = 77%
Test for overall effect: Z = 2.20 (P = 0.03)



C

Study or Subgroup	SILA Events	SILA Total	TPLA Events	TPLA Total	Weight	Risk Ratio M-H, Fixed, 95% CI	Year
Park 2010	1	20	0	20	1.9%	3.00 [0.13, 69.52]	2010
Teoh 2012	14	100	18	100	67.9%	0.78 [0.41, 1.48]	2012
Lee 2013	5	124	8	124	30.2%	0.63 [0.21, 1.86]	2013
Total (95% CI)		**244**		**244**	**100.0%**	**0.77 [0.45, 1.33]**	
Total events	20		26				

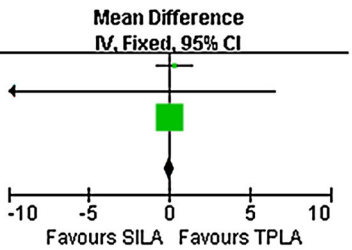
Heterogeneity: Chi² = 0.86, df = 2 (P = 0.65); I² = 0%
Test for overall effect: Z = 0.93 (P = 0.35)



D

Study or Subgroup	SILA Mean	SILA SD	SILA Total	TPLA Mean	TPLA SD	TPLA Total	Weight	Mean Difference IV, Fixed, 95% CI	Year
St. Peter 2011	7.2	5.1	180	6.9	5.2	180	8.9%	0.30 [-0.76, 1.36]	2011
Teoh 2012	52.8	24.96	100	71.76	127.44	100	0.0%	-18.96 [-44.41, 6.49]	2012
Sozutek 2013	6.3	0.6	25	6.3	0.6	25	91.1%	0.00 [-0.33, 0.33]	2013
Total (95% CI)			**305**			**305**	**100.0%**	**0.02 [-0.29, 0.34]**	

Heterogeneity: Chi² = 2.42, df = 2 (P = 0.30); I² = 17%
Test for overall effect: Z = 0.15 (P = 0.88)



◀**Fig. 3** **A** Extra trocars placed during SILA and TPLA techniques, showing higher likelihood of events for SILA. **B** Extra trocars placed during SILA and TPLA (risk difference calculated). **C** Drainages inserted during SILA and TPLA, showing comparable requirement. **D** Time to regular diet post SILA and TPLA, indicating similar results. *SILA* single-incision laparoscopic appendectomy, *TPLA* three-port laparoscopic appendectomy

no longer existed when only considering studies including pregnancy (3RCTs; 37 vs 32; WMD: 5.84; 95 % CI −0.79 to 12.46; $P = 0.08$; Fig. 6A) and perforation (4RCTs; 36 vs 34; WMD: 4.47; 95 % CI −2.80 to 11.74; $P = 0.23$; Fig. 6B), and with less than 150 cases (4RCTs; 43 vs 38; WMD: 5.92; 95 % CI −0.97 to 12.82; $P = 0.09$; Fig. 6C), with significant intergroup heterogeneity observed though. The overall, major and minor surgical complications, and wound infections remained comparable between SILA and TPLA with low heterogeneity for all subgroups evaluated. Discrepancy in extra trocars persisted in both subgroups with pregnancy included and excluded (Fig. 6D), but disappeared when only including perforated cases (2RCTs; 3 vs 0 %; RR: 3.00; 95 % CI 0.32–28.14; $P = 0.34$; Fig. 6E) and when there were less than 150 cases (3RCTs; 3 vs 0 %; RR: 3.00; 95 % CI 0.48 to 18.58; $P = 0.24$; Fig. 6F).

Sensitivity analysis for subgroups was further conducted, and we found that with Kye's data excluded, SILA took longer again both when pregnancy was included in calculation (37 vs 40; WMD: 8.78; 95 % CI 2.32–15.25; $P = 0.008$; Fig. 7A) and when sample size was less than 150 (47 vs 38; WMD: 8.34; 95 % CI 2.00–14.68; $P = 0.01$; Fig. 7B). Without Lee's data, two procedures were accompanied with comparable extra trocars addressed when pregnancy (2 vs 0 %; RR: 3.02; 95 % CI 0.49–18.75; $P = 0.24$; Fig. 7C) was excluded in analysis.

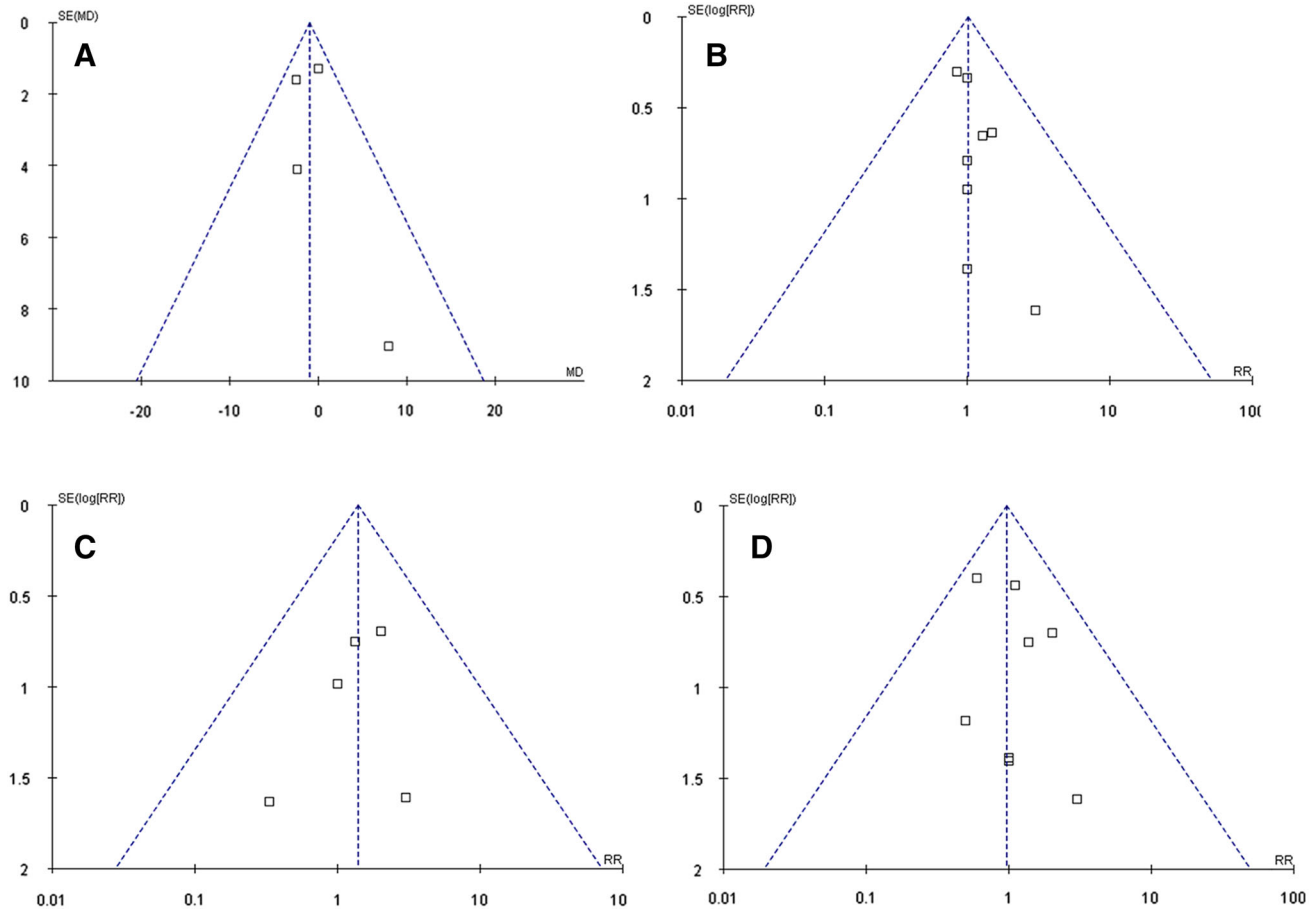


Fig. 4 Funnel plots for **A** hospital duration, **B** overall complications, **C** major surgical complications, **D** minor surgical complications, **E** ileus, **F** abdominal infections, **G** wound infections, and **H** extra trocars required between two procedures, showing that all parameters are free from significant bias

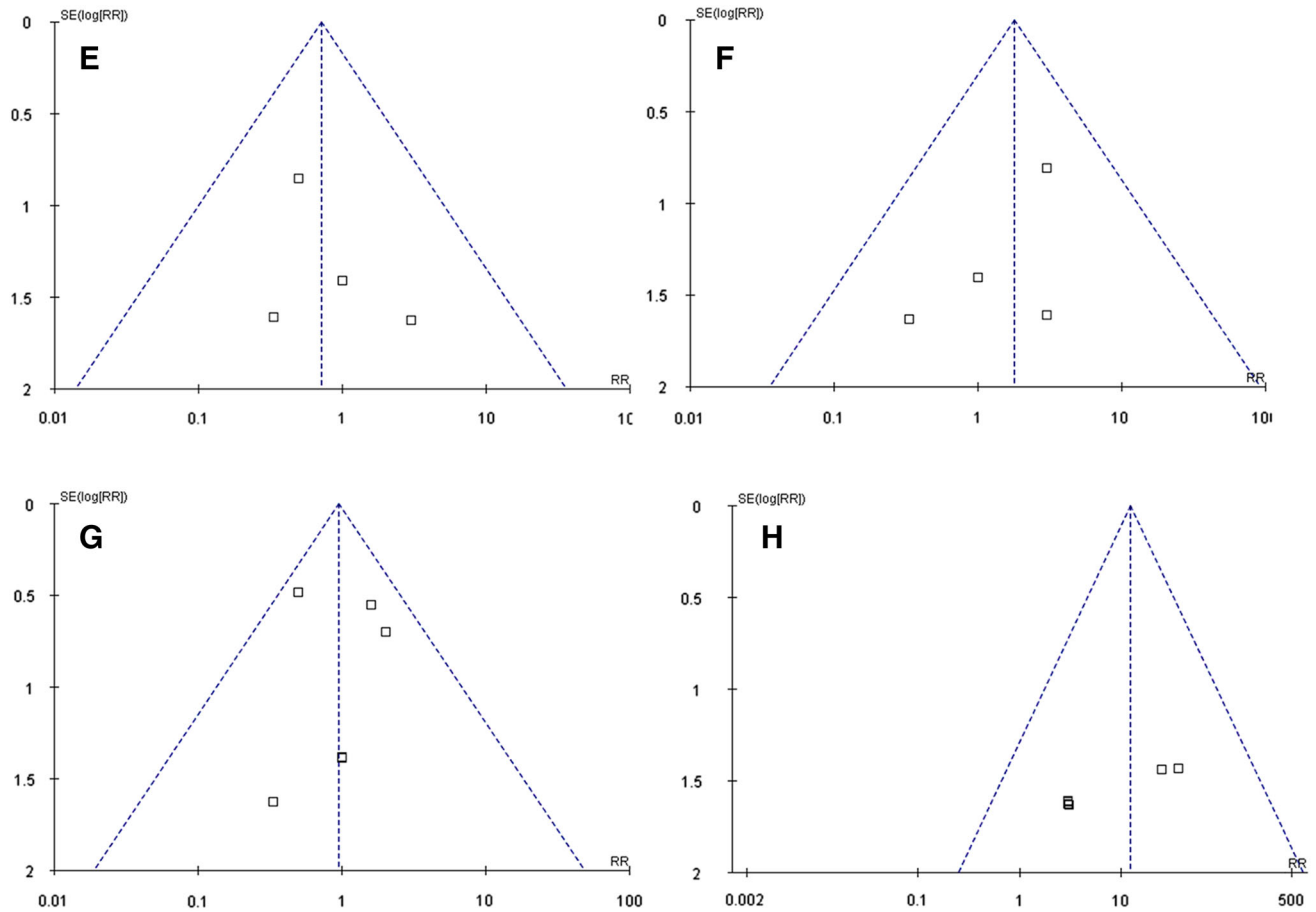


Fig. 4 continued

Discussion

LA has been proposed to reduce the invasiveness of appendectomy, and was first applied to cure AA by Schreiber [35] in 1987. Although the open procedure is still used in some medical centers and there may exist conversions during LA, the superior clinical outcomes of LA has been certified by convincing proves, and many surgical institutions are inclined to LA because of availability of whole abdominal cavity profilering especially among fat and pregnant population [3–5]. SILA is developing and gaining popularity rapidly with its unique benefit of concealing surgical wound within the umbilicus [36]. There havve been many trials evaluating this new technique mainly among selective adults and uncomplicated AA sufferers without perforation or abscess and many reported ideal achievements [6, 8]. However, most of reports are limited to nonrandomized retrospective study based on relatively small population and focus on the aspect of operating technique [37].

Six systematic reviews based on mainly non-RCTs concluded that SILA was comparable to TPLA in safety and effectiveness [9–14]. Compared with the previous studies, our analyses share some similarities. But the quality of non-RCTs has a great impact on the accuracy of pooled estimates, and the previous meta-analyses comparing SILA with TPLA may contain duplicate and incomplete studies, thus leading to great bias.

This study summarizes the highest quality data comparing SILA with TPLA. In our analysis, RCTs were all published after 2009, and those published in 2013 constituted most of the studies included, which are not included in most previous meta-analyses. Some of the individual trials were inconclusive as they were underpowered and hence too small to identify significant differences regarding the important determinants of ideal LA. This meta-analysis aims to provide this evidence.

Surgical techniques of the included trials were standardized. Three trials enrolled a comparable number of patients suffering from perforated AA and pregnancy in

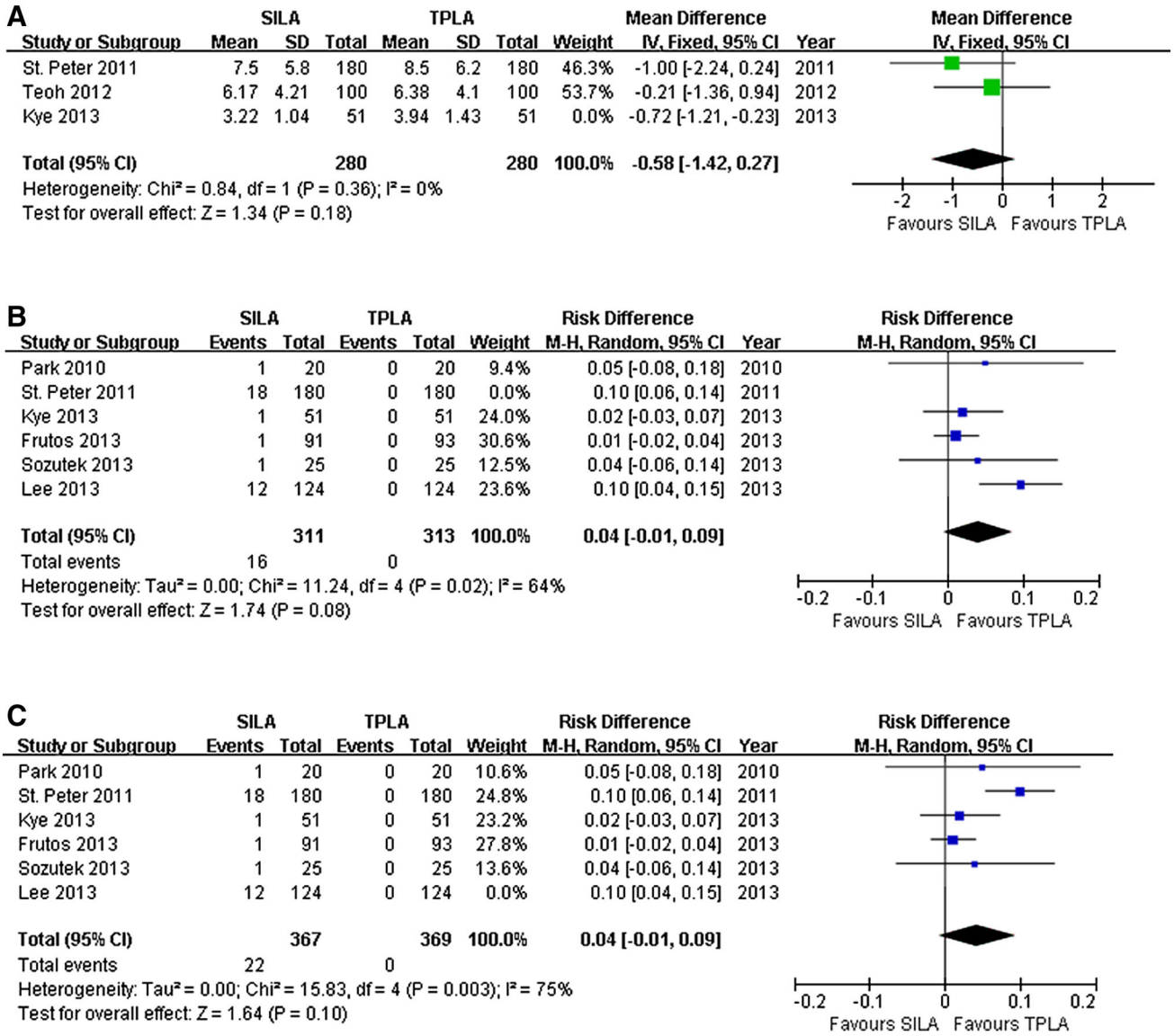


Fig. 5 **A** Sensitivity test for days to full activities after SILA and TPLA, showing the difference disappears disregarding Kye's study. **B** Extra trocars applied during SILA and TPLA techniques ignoring St. Peter's result and **C** Lee's report, both showing comparative results when risk difference is calculated. *SILA* single-incision laparoscopic appendectomy, *TPLA* three-port laparoscopic appendectomy

both arms. Study population was similar between trials in all mentioned aspects.

Researches of different qualities revealed discrepant comparisons of surgical duration between the 2 techniques, and most reported longer operating time during SILA [28]. However, in surgical centers majored in this technique, SILA could consume shorter time; [38] Ding's [11] pooled result based on mainly retrospective studies showed no difference. Our results showed that operative time increased significantly by approximately 5 min in the SILA group, which is not an appreciable clinical difference though. Although SILA seems more difficult than TPLA to conduct technically with a limited vision [28], it may be more practicable when placing gauzes and cleaning abdominal cavity, and the conflicts of external instruments and limitation of their movements caused by parallel and approaching of apparatus which makes adequate triangulation of traction and counter-traction difficult can be solved by improvement of equipment [6]. With joint efforts of surgeons and academic centers, improvements in instrumentation like angled or flexible endoscopes and in ergonomics, and maturation and modification of the new

Table 10 Subgroup analysis for selected RCTs

Subgroup/outcome	No. studies	No. patients		WMD/RR	95 % CI	*P*	HG χ^2	HG *P*
		SILA	TPLA					
Operative time (min)								
Pregnancy included	3	256	256	5.84	−0.79 to 12.46	0.08	29.55	<0.00001
Pregnancy excluded	5	360	362	5.77	3.45 to 8.08	<0.00001	3.36	0.50
Perforation included	4	201	201	4.47	−2.80 to 11.74	0.23	30.33	<0.00001
Perforation excluded	4	415	417	6.21	4.25 to 8.16	<0.00001	1.50	0.68
<150 cases	4	121	121	5.92	−0.97 to 12.82	0.09	27.45	<0.00001
>150 cases	4	495	497	5.81	3.86 to 7.77	<0.00001	1.35	0.72
Overall complications								
Pregnancy included	3	256	256	1.40	0.56–3.51	0.47	0.42	0.81
Pregnancy excluded	5	360	362	0.95	0.64–1.43	0.82	0.37	0.99
Perforation included	3	101	101	1.22	0.36–4.12	0.75	0.40	0.82
Perforation excluded	5	515	517	1.00	0.68–1.48	0.99	0.83	0.93
<150 cases	4	121	121	1.15	0.42–3.19	0.78	0.42	0.94
>150 cases	4	495	497	1.00	0.67–1.49	0.99	0.83	0.84
Major surgical complications								
Pregnancy included	3	256	256	0.71	0.14–3.54	0.68	0.34	0.56
Pregnancy excluded	5	360	362	1.77	0.69–4.55	0.24	0.28	0.87
Perforation included	4	201	201	1.20	0.37–3.85	0.76	0.05	0.82
Perforation excluded	4	415	417	1.60	0.53–4.81	0.40	1.18	0.55
<150 cases	4	121	121	1.40	0.28–6.88	0.68	0.34	0.56
>150 cases	4	495	497	1.40	0.56–3.52	0.47	1.04	0.59
Minor surgical complications								
Pregnancy included	3	256	256	1.89	0.61–5.84	0.27	0.30	0.86
Pregnancy excluded	5	360	362	0.84	0.50–1.39	0.49	1.73	0.78
Perforation included	4	201	201	1.17	0.55–2.50	0.68	0.38	0.94
Perforation excluded	4	415	417	0.87	0.49–1.56	0.64	2.85	0.42
<150 cases	4	121	121	1.00	0.28–3.59	1.00	0.81	0.85
>150 cases	4	495	497	0.97	0.59–1.58	0.90	2.80	0.42
Wound infections								
Pregnancy included	3	256	256	1.44	0.44–4.75	0.54	1.03	0.31
Pregnancy excluded	4	269	269	0.84	0.44–1.60	0.60	2.54	0.47
Perforation included	4	201	201	1.27	0.50–3.21	0.62	0.89	0.64
Perforation excluded	3	324	324	0.81	0.40–1.66	0.57	2.69	0.26
<150 cases	4	121	121	0.71	0.15–3.52	0.68	0.34	0.84
>150 cases	3	404	404	1.00	0.55–1.83	1.00	3.76	0.15
Extra trocars								
Pregnancy included	2	231	231	20.00	2.70–148.09	0.003	1.55	0.21
Pregnancy excluded	4	260	262	8.53	1.99–36.62	0.0004	1.80	0.61
Perforation included	2	76	76	3.00	0.32–28.14	0.34	0.00	1.00
Perforation excluded	4	415	417	17.05	4.11–70.69	<0.0001	2.65	0.45
<150 cases	3	96	96	3.00	0.48–18.58	0.24	0.00	1.00
>150 cases	3	491	493	21.76	4.25–111.49	0.0002	1.60	0.45

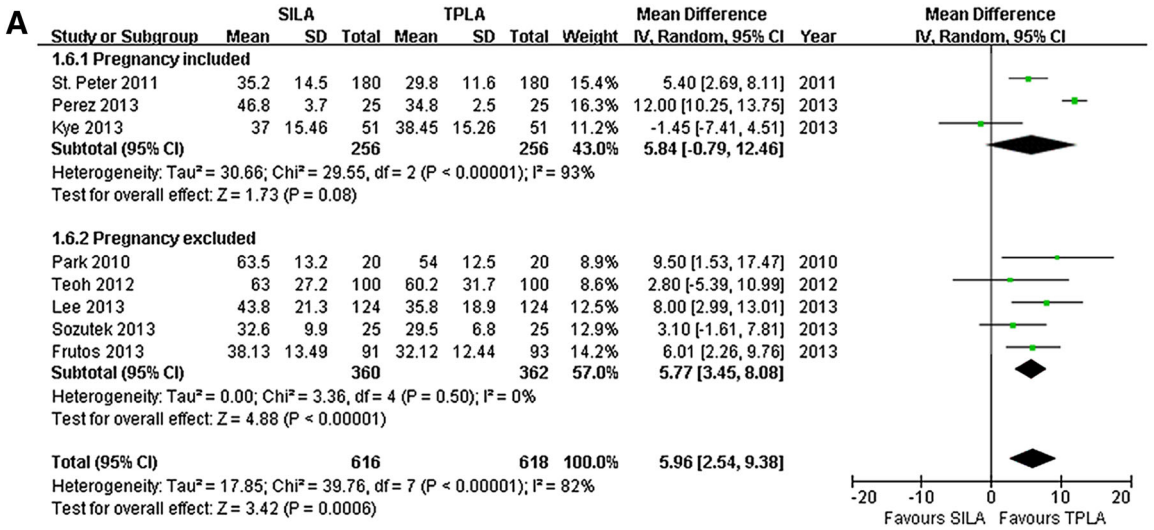
RCTs randomized controlled trials, *SILA* single-incision laparoscopic appendectomy, *TPLA* three-port laparoscopic appendectomy, *RR* risk ratio, *WMD* weighted mean difference, *CI* confidence interval, *HG* Higgins

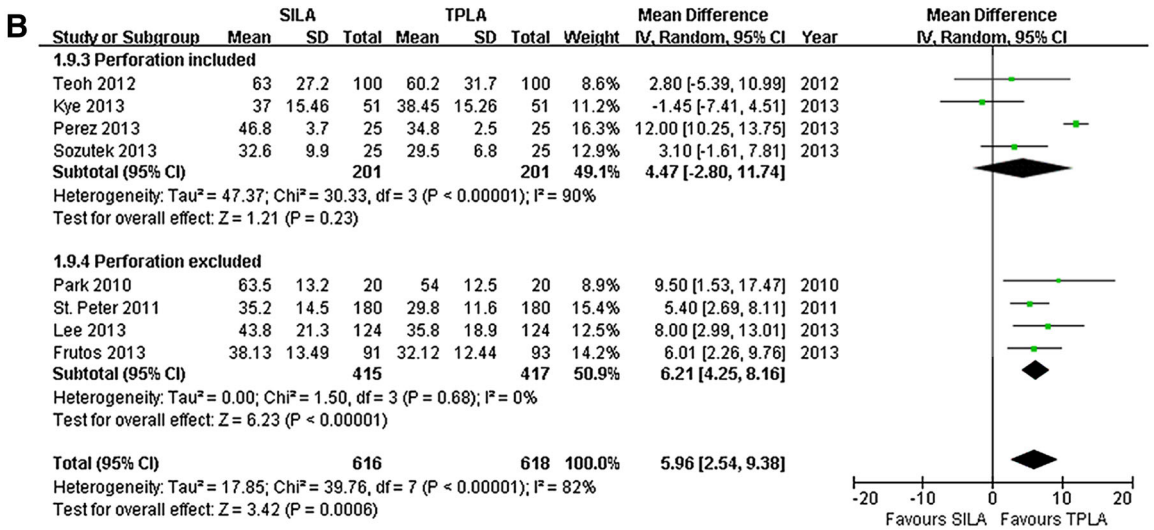
technique, it is reasonable to believe that conducting SILA may consume less and less time with a wider diffusion of this technique, but may require a long and steep learning curve, and good cooperation of whole therapeutic team [6, 8]. We believe that SILA for AA should be offered only in large specialized centers with experience in SILA procedures and a large number of patients in order to make this learning curve completed more effectively. Several of the studies included in our analysis reported on their initial experience, so some outcomes studied, including operative time may have been influenced by learning curve issues. The technical change from conventional to single-port LA requires a learning curve of at least 10 surgeries for a basic handling of SILA [39]. Unfortunately, most studies did not explicitly describe their previous level of proficiency with the technique, so we were unable to perform a subgroup analysis that directly addressed this matter. As a surrogate, a subgroup analysis was performed using 150 cases as a cut point, but the change of SILA operative time was not significant, and the time was still longer than TPLA. It is likely that we did not observe a more pronounced effect of the number of SILA cases performed because the studies represented, for the large part, the experience of a group of surgeons, whereas the learning curve is an individual achievement. In difficult cases like perforation, TPLA may promise more expeditious and easier dissection and mobilization [28]. We did not found significant difference in surgical time when dealing with pure perforated AA cases, and pooled analysis based on studies in which pregnancy or perforated AA was included revealed similar results between 2 procedures.

Recently, the results of RCTs demonstrated that SILA resulted in similar post-surgical complications compared with TPLA, and trials of larger scale reported no greater complication rates during SILA than those revealed before [40]. The level 1a evidence provided by us showed no significant differences as to overall, surgical (major and minor), and medical complications between 2 techniques, which may be because SILA, although less trocars applied, leads to the same organ and mesoappendix resection as TPLA. SILA with insertion of just 1 trocar in the umbilical area eliminates the possibility of injury to the bladder and the inferior epigastric vessels [8]. Wound complications seem to be common for LA [8, 28], and early reports indicated SILA might be combined with higher incidence of wound infection [8]. According to the best evidence provided by us, there is no significant difference on this issue regardless of specific protection for umbilical skin during appendix division [28], and the discrepancy shown before might be due to diverse surgical techniques and postsurgical management. Theoretically, the larger abdominal incision is, the higher risk of postoperative hernias there will be. Based on the included RCTs, we found basically no existence. Rates of ileus, abdominal infection and reoperation were all similar between SILA and TPLA techniques according to our convincing analysis. Period of post-surgical follow-ups may be a great influential factor impacting complication rates especially the long-terms though. Our study also revealed that SILA significantly required an extra port in only 7 % of cases during surgery, which is not clinically significant though. And in the case of inadequate visualization or mobilization of the appendix, the insertion of additional ports or trocars is not regarded as a shortcoming but is supported to preserve the appropriateness of the operation [40]. We further revealed that during complicated AA managing, comparable trocars were required in both procedures. Our pooled results showed that patients undergoing two procedures required comparable drains at the end of LA, which may be a challenge for SILA because the placement of a drain via the umbilicus may lead to higher risk of wound infection and incisional hernia, and affect cosmetic results [8].

With comparable usage of analgesics and anti-inflammatory drugs, it is believed that the larger the transumbilical fascial incision is and the greater wound irritation there exists due to the insertion of all surgical instruments through only one incision, the more painful patients may experience post-LA [28]. While others demonstrated that postsurgical pain is mainly related to the injury of muscles and parietal peritoneum, regardless of the diameter of the trocar, and that for minimally invasive surgery, the less trocars, the less pain [41]. Patients may suffer from more serious pain post SILA, while other researchers made the converse conclusion [28]. We found that 12 and 24 h VAS scores were comparable post 2 procedures, possibly because there is only 1 trocar during SILA through which all equipment has to be inserted, thus size may not reduce significantly compared with the sum of the 3 trocars when performing TPLA [28]. Researches showed better postoperative recovery results after SILA than those after TPLA [27–34]. Ding [11] revealed shorter length of hospital stay for SILA, but we showed no significant difference on this issue. We also revealed comparable perioperative recovery parameters between 2 procedures including time to regular diet, and postsurgical hospital stay. Though patients undergoing SILA could return to full activities earlier according to our convincing results, but it is not a clinically distinction actually due to the interval of observation.

The internal validity of this study is high because the analysis was based on high-quality RCTs, with low risk of bias. This analysis is limited by the diverse follow-up period and the fact that not all outcomes of interest are reported by all enrolled studies. One RCT [25] is currently being conducted in England, and it is hoped that it will address questions better.


A
SILA
TPLA
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI Year
IV, Random, 95% CI
1.6.1 Pregnancy included
St. Peter 2011 35.2 14.5 180 29.8 11.6 180 15.4% 5.40 [2.69, 8.11] 2011
Perez 2013 46.8 3.7 25 34.8 2.5 25 16.3% 12.00 [10.25, 13.75] 2013
Kye 2013 37 15.46 51 38.45 15.26 51 11.2% -1.45 [-7.41, 4.51] 2013
Subtotal (95% CI) 256 256 43.0% 5.84 [-0.79, 12.46]
Heterogeneity: Tau² = 30.66; Chi² = 29.55, df = 2 (P < 0.00001); I² = 93%
Test for overall effect: Z = 1.73 (P = 0.08)
1.6.2 Pregnancy excluded
Park 2010 63.5 13.2 20 54 12.5 20 8.9% 9.50 [1.53, 17.47] 2010
Teoh 2012 63 27.2 100 60.2 31.7 100 8.6% 2.80 [-5.39, 10.99] 2012
Lee 2013 43.8 21.3 124 35.8 18.9 124 12.5% 8.00 [2.99, 13.01] 2013
Sozutek 2013 32.6 9.9 25 29.5 6.8 25 12.9% 3.10 [-1.61, 7.81] 2013
Frutos 2013 38.13 13.49 91 32.12 12.44 93 14.2% 6.01 [2.26, 9.76] 2013
Subtotal (95% CI) 360 362 57.0% 5.77 [3.45, 8.08]
Heterogeneity: Tau² = 0.00; Chi² = 3.36, df = 4 (P = 0.50); I² = 0%
Test for overall effect: Z = 4.88 (P < 0.00001)
Total (95% CI) 616 618 100.0% 5.96 [2.54, 9.38]
Heterogeneity: Tau² = 17.85; Chi² = 39.76, df = 7 (P < 0.00001); I² = 82%
Test for overall effect: Z = 3.42 (P = 0.0006)
-20 -10 0 10 20
Favours SILA Favours TPLA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SILA
TPLA
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI Year
IV, Random, 95% CI
1.9.3 Perforation included
Teoh 2012 63 27.2 100 60.2 31.7 100 8.6% 2.80 [-5.39, 10.99] 2012
Kye 2013 37 15.46 51 38.45 15.26 51 11.2% -1.45 [-7.41, 4.51] 2013
Perez 2013 46.8 3.7 25 34.8 2.5 25 16.3% 12.00 [10.25, 13.75] 2013
Sozutek 2013 32.6 9.9 25 29.5 6.8 25 12.9% 3.10 [-1.61, 7.81] 2013
Subtotal (95% CI) 201 201 49.1% 4.47 [-2.80, 11.74]
Heterogeneity: Tau² = 47.37; Chi² = 30.33, df = 3 (P < 0.00001); I² = 90%
Test for overall effect: Z = 1.21 (P = 0.23)
1.9.4 Perforation excluded
Park 2010 63.5 13.2 20 54 12.5 20 8.9% 9.50 [1.53, 17.47] 2010
St. Peter 2011 35.2 14.5 180 29.8 11.6 180 15.4% 5.40 [2.69, 8.11] 2011
Lee 2013 43.8 21.3 124 35.8 18.9 124 12.5% 8.00 [2.99, 13.01] 2013
Frutos 2013 38.13 13.49 91 32.12 12.44 93 14.2% 6.01 [2.26, 9.76] 2013
Subtotal (95% CI) 415 417 50.9% 6.21 [4.25, 8.16]
Heterogeneity: Tau² = 0.00; Chi² = 1.50, df = 3 (P = 0.68); I² = 0%
Test for overall effect: Z = 6.23 (P < 0.00001)
Total (95% CI) 616 618 100.0% 5.96 [2.54, 9.38]
Heterogeneity: Tau² = 17.85; Chi² = 39.76, df = 7 (P < 0.00001); I² = 82%
Test for overall effect: Z = 3.42 (P = 0.0006)
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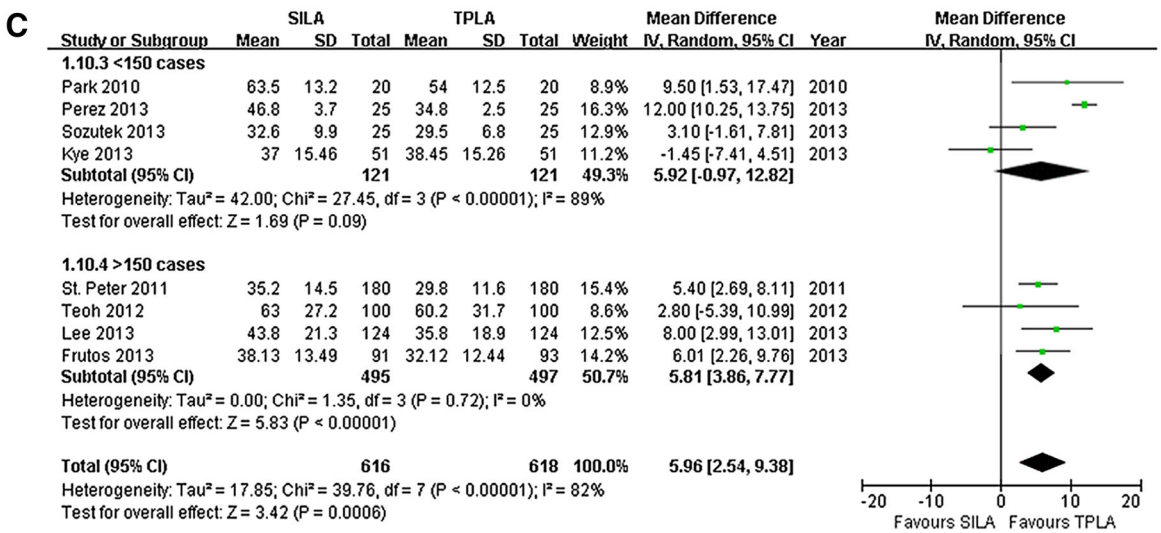
Favours SILA Favours TPLA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SILA
TPLA
Mean Difference
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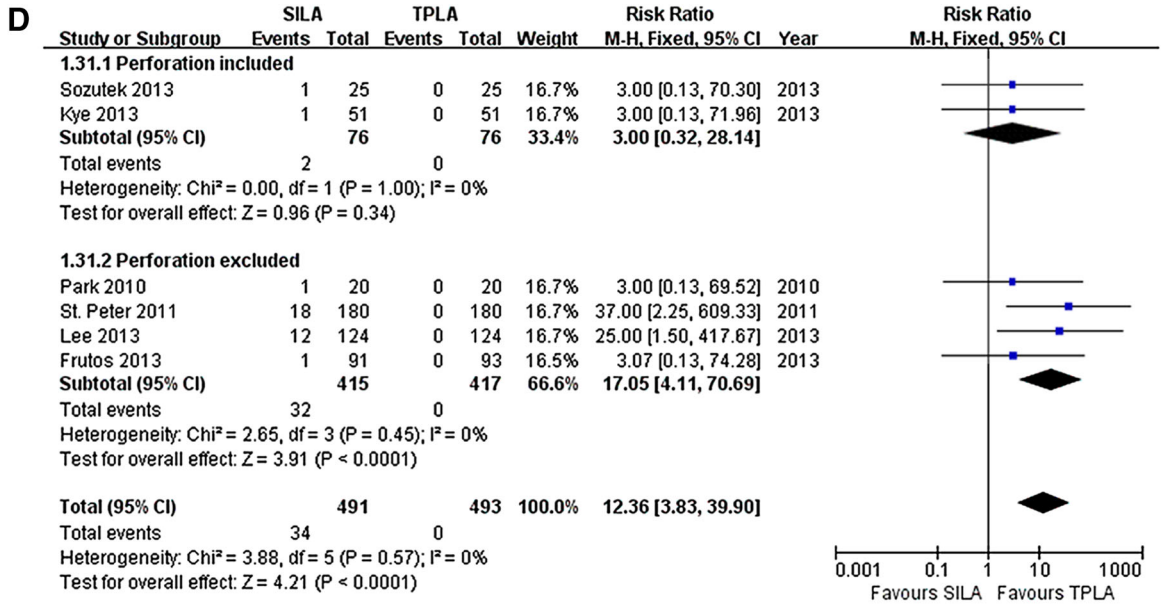
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI Year
IV, Random, 95% CI
1.10.3 <150 cases
Park 2010 63.5 13.2 20 54 12.5 20 8.9% 9.50 [1.53, 17.47] 2010
Perez 2013 46.8 3.7 25 34.8 2.5 25 16.3% 12.00 [10.25, 13.75] 2013
Sozutek 2013 32.6 9.9 25 29.5 6.8 25 12.9% 3.10 [-1.61, 7.81] 2013
Kye 2013 37 15.46 51 38.45 15.26 51 11.2% -1.45 [-7.41, 4.51] 2013
Subtotal (95% CI) 121 121 49.3% 5.92 [-0.97, 12.82]
Heterogeneity: Tau² = 42.00; Chi² = 27.45, df = 3 (P < 0.00001); I² = 89%
Test for overall effect: Z = 1.69 (P = 0.09)
1.10.4 >150 cases
St. Peter 2011 35.2 14.5 180 29.8 11.6 180 15.4% 5.40 [2.69, 8.11] 2011
Teoh 2012 63 27.2 100 60.2 31.7 100 8.6% 2.80 [-5.39, 10.99] 2012
Lee 2013 43.8 21.3 124 35.8 18.9 124 12.5% 8.00 [2.99, 13.01] 2013
Frutos 2013 38.13 13.49 91 32.12 12.44 93 14.2% 6.01 [2.26, 9.76] 2013
Subtotal (95% CI) 495 497 50.7% 5.81 [3.86, 7.77]
Heterogeneity: Tau² = 0.00; Chi² = 1.35, df = 3 (P = 0.72); I² = 0%
Test for overall effect: Z = 5.83 (P < 0.00001)
Total (95% CI) 616 618 100.0% 5.96 [2.54, 9.38]
Heterogeneity: Tau² = 17.85; Chi² = 39.76, df = 7 (P < 0.00001); I² = 82%
Test for overall effect: Z = 3.42 (P = 0.0006)
-20 -10 0 10 20
Favours SILA Favours TPLA

◀**Fig. 6** **A** Subgroup analysis for surgical duration according to whether pregnancy or **B** perforation is included and **C** by using a 150 cases cut-point, showing difference no longer exists when only considering studies including pregnancy (**A**) and perforation (**B**) and with less than 150 cases (**C**). Subgroup analysis for extra trocars according to whether perforation is included (**D**) and by using a 150 cases cut-point (**E**), showing difference disappears when only considering studies including perforation (**D**) and with less than 150 cases (**E**)

In conclusion, choice of the technique for AA may be based on patients' preferences and presence of local expertise [29]. SILA is basically a comparable option for the treatment of AA that compares favorably with TPLA in hospital stay and post-operative complications. Statistically, SILA results in a longer operative duration and require more extra trocars, while patients could return to normal activities earlier post-SILA. However, these differences are not clinically significant, and may be due to learning curve issues. All other indexes are similar. More studies are needed to be carried out in patients suffering from complicated AA and those with higher BMI and associated comorbidities. These results lend level 1a support for the alternative use of SILA for the surgical treatment of AA.



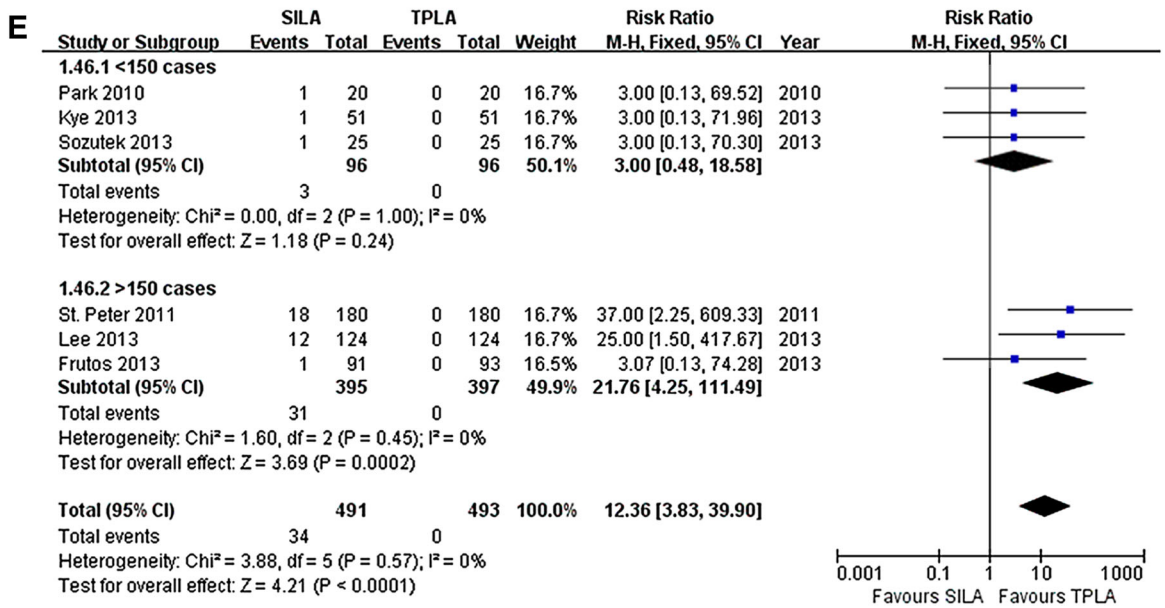
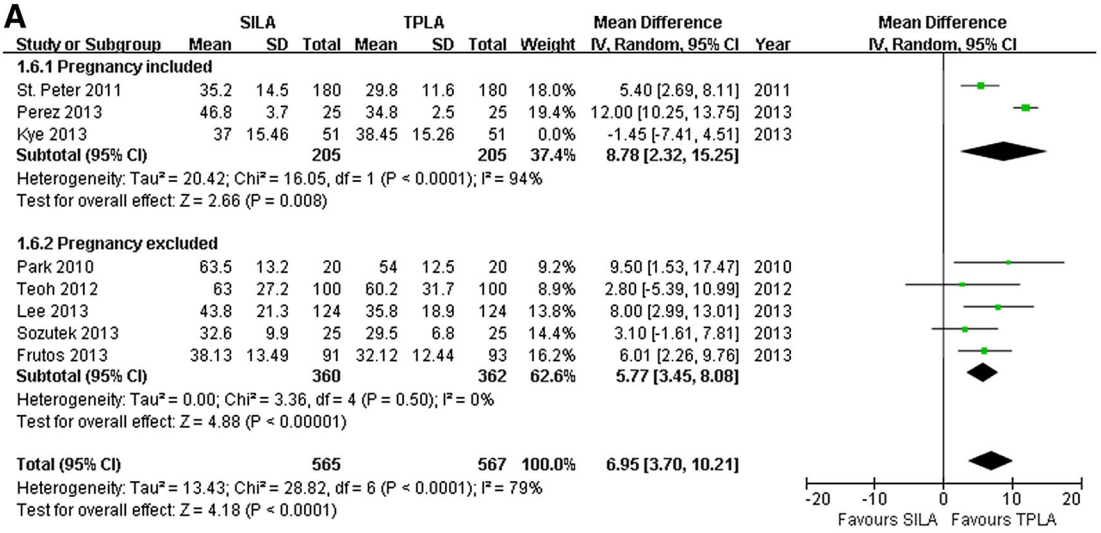
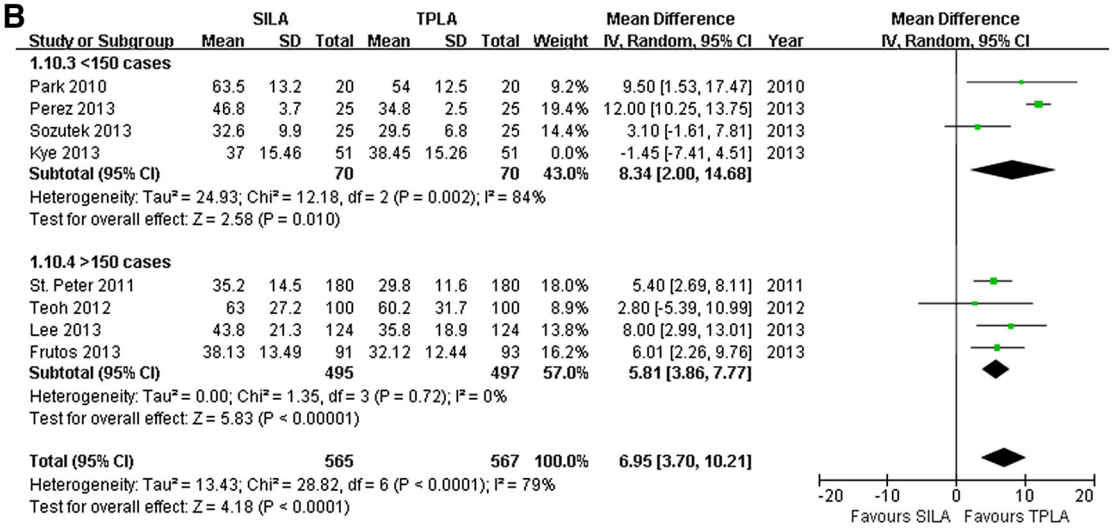


Fig. 6 continued

A


SILA
TPLA
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI Year
IV, Random, 95% CI
1.6.1 Pregnancy included
St. Peter 2011 35.2 14.5 180 29.8 11.6 180 18.0% 5.40 [2.69, 8.11] 2011
Perez 2013 46.8 3.7 25 34.8 2.5 25 19.4% 12.00 [10.25, 13.75] 2013
Kye 2013 37 15.46 51 38.45 15.26 51 0.0% -1.45 [-7.41, 4.51] 2013
Subtotal (95% CI) 205 205 37.4% 8.78 [2.32, 15.25]
Heterogeneity: Tau² = 20.42; Chi² = 16.05, df = 1 (P < 0.0001); I² = 94%
Test for overall effect: Z = 2.66 (P = 0.008)
1.6.2 Pregnancy excluded
Park 2010 63.5 13.2 20 54 12.5 20 9.2% 9.50 [1.53, 17.47] 2010
Teoh 2012 63 27.2 100 60.2 31.7 100 8.9% 2.80 [-5.39, 10.99] 2012
Lee 2013 43.8 21.3 124 35.8 18.9 124 13.8% 8.00 [2.99, 13.01] 2013
Sozutek 2013 32.6 9.9 25 29.5 6.8 25 14.4% 3.10 [-1.61, 7.81] 2013
Frutos 2013 38.13 13.49 91 32.12 12.44 93 16.2% 6.01 [2.26, 9.76] 2013
Subtotal (95% CI) 360 362 62.6% 5.77 [3.45, 8.08]
Heterogeneity: Tau² = 0.00; Chi² = 3.36, df = 4 (P = 0.50); I² = 0%
Test for overall effect: Z = 4.88 (P < 0.00001)
Total (95% CI) 565 567 100.0% 6.95 [3.70, 10.21]
Heterogeneity: Tau² = 13.43; Chi² = 28.82, df = 6 (P < 0.0001); I² = 79%
Test for overall effect: Z = 4.18 (P < 0.0001)
-20 -10 0 10 20
Favours SILA Favours TPLA

B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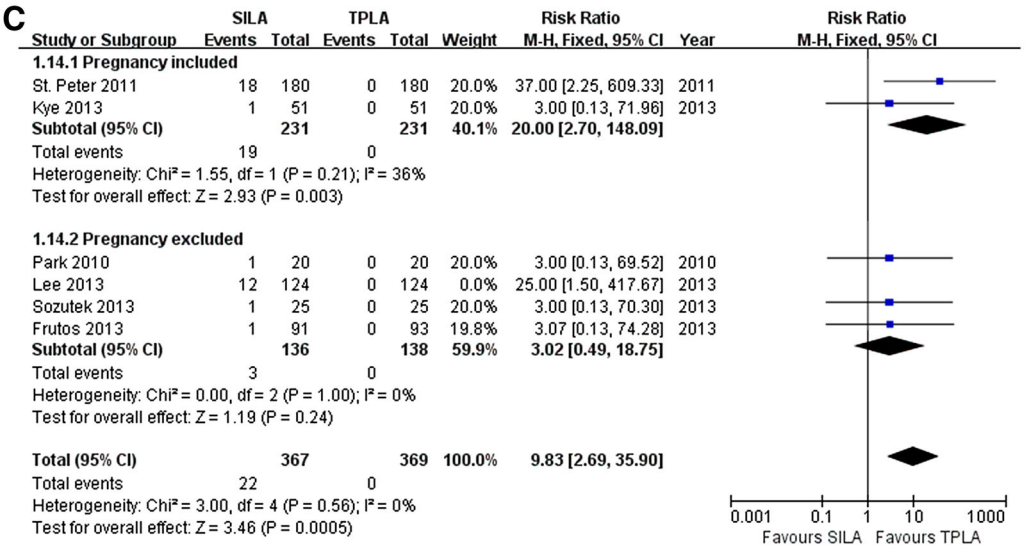
TPLA
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI Year
IV, Random, 95% CI
1.10.3 <150 cases
Park 2010 63.5 13.2 20 54 12.5 20 9.2% 9.50 [1.53, 17.47] 2010
Perez 2013 46.8 3.7 25 34.8 2.5 25 19.4% 12.00 [10.25, 13.75] 2013
Sozutek 2013 32.6 9.9 25 29.5 6.8 25 14.4% 3.10 [-1.61, 7.81] 2013
Kye 2013 37 15.46 51 38.45 15.26 51 0.0% -1.45 [-7.41, 4.51] 2013
Subtotal (95% CI) 70 70 43.0% 8.34 [2.00, 14.68]
Heterogeneity: Tau² = 24.93; Chi² = 12.18, df = 2 (P = 0.002); I² = 84%
Test for overall effect: Z = 2.58 (P = 0.010)
1.10.4 >150 cases
St. Peter 2011 35.2 14.5 180 29.8 11.6 180 18.0% 5.40 [2.69, 8.11] 2011
Teoh 2012 63 27.2 100 60.2 31.7 100 8.9% 2.80 [-5.39, 10.99] 2012
Lee 2013 43.8 21.3 124 35.8 18.9 124 13.8% 8.00 [2.99, 13.01] 2013
Frutos 2013 38.13 13.49 91 32.12 12.44 93 16.2% 6.01 [2.26, 9.76] 2013
Subtotal (95% CI) 495 497 57.0% 5.81 [3.86, 7.77]
Heterogeneity: Tau² = 0.00; Chi² = 1.35, df = 3 (P = 0.72); I² = 0%
Test for overall effect: Z = 5.83 (P < 0.00001)
Total (95% CI) 565 567 100.0% 6.95 [3.70, 10.21]
Heterogeneity: Tau² = 13.43; Chi² = 28.82, df = 6 (P < 0.0001); I² = 79%
Test for overall effect: Z = 4.18 (P < 0.0001)
-20 -10 0 10 20
Favours SILA Favours TPLA

C


SILA
TPLA
Risk Ratio
Risk Ratio
Study or Subgroup Events Total Events Total Weight M-H, Fixed, 95% CI Year
M-H, Fixed, 95% CI
1.14.1 Pregnancy included
St. Peter 2011 18 180 0 180 20.0% 37.00 [2.25, 609.33] 2011
Kye 2013 1 51 0 51 20.0% 3.00 [0.13, 71.96] 2013
Subtotal (95% CI) 231 231 40.1% 20.00 [2.70, 148.09]
Total events 19 0
Heterogeneity: Chi² = 1.55, df = 1 (P = 0.21); I² = 36%
Test for overall effect: Z = 2.93 (P = 0.003)
1.14.2 Pregnancy excluded
Park 2010 1 20 0 20 20.0% 3.00 [0.13, 69.52] 2010
Lee 2013 12 124 0 124 0.0% 25.00 [1.50, 417.67] 2013
Sozutek 2013 1 25 0 25 20.0% 3.00 [0.13, 70.30] 2013
Frutos 2013 1 91 0 93 19.8% 3.07 [0.13, 74.28] 2013
Subtotal (95% CI) 136 138 59.9% 3.02 [0.49, 18.75]
Total events 3 0
Heterogeneity: Chi² = 0.00, df = 2 (P = 1.00); I² = 0%
Test for overall effect: Z = 1.19 (P = 0.24)
Total (95% CI) 367 369 100.0% 9.83 [2.69, 35.90]
Total events 22 0
Heterogeneity: Chi² = 3.00, df = 4 (P = 0.56); I² = 0%
Test for overall effect: Z = 3.46 (P = 0.0005)
0.001 0.1 1 10 1000
Favours SILA Favours TPLA

◀**Fig. 7** Sensitivity tests for subgroups of operative time according to whether pregnancy is included (**A**) and by using a 150 cases cut-point (**B**), showing both differences recur when Kye's study is excluded in the subgroups including pregnancy (**A**) and with less than 150 cases (**B**), respectively. **C** Sensitivity test for subgroups of extra trocars placed according to whether pregnancy is included, showing difference emerges when Lee's results is excluded in the subgroups excluding pregnancy

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