

# Bayesian network meta-analysis of the effects of single-incision laparoscopic surgery, conventional laparoscopic appendectomy and open appendectomy for the treatment of acute appendicitis

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Received September 28, 2016; Accepted June 16, 2017

DOI: 10.3892/etm.2017.5343

**Abstract.** The present study aimed to systematically evaluate the effectiveness of single-incision laparoscopic surgery (SILS), conventional laparoscopic appendectomy (CLA) and open appendectomy (OA) for the treatment of acute appendicitis. PubMed and Embase databases were systematically searched to identify relevant studies comparing the effectiveness of different appendectomy methods for treating acute appendicitis published prior to April 2016. ADDIS 1.16.5 software was used for data analysis. Heterogeneity was assessed using  $I^2$  statistic. Odds ratios or standardized mean differences and 95% confidence intervals were calculated and pooled accordingly. Consistency was assessed using node-splitting analysis and inconsistency standard deviation. Convergence was assessed with the Brooks-Gelman-Rubin method using Potential Scale Reduction Factor (PSRF). Surgical procedure duration, duration of hospital stay, wound infection and incidence of abscesses were compared. A total of 24 eligible studies were included in this meta-analysis. A consistency model was used to pool data regarding the four outcomes. The PSRFs in each item were all  $<1.03$ . Pooled results showed that, compared with OA, SILS and CLA were associated with significantly shorter durations of hospital stay (all  $P<0.01$ ) and lower risk of wound infection (SILS vs. OA  $P=0.02$  and CLA vs. OA  $P<0.01$ , respectively), but no significant differences were identified between SILS and CLA. However, compared with OA, SILS exhibited a significantly longer surgical procedure duration ( $P=0.01$ ) and lower incidence of abscesses ( $P=0.04$ ), while no significant difference was observed between OA and

CLA. This comprehensive network meta-analysis indicated that laparoscopic appendectomy, including SILS and CLA, may have more advantages for acute appendicitis compared with OA. Furthermore, SILS procedures require improvement and simplification to reduce the surgical procedure duration.

## Introduction

Acute appendicitis is a common acute abdominal condition and the conventional treatment is excision (1). There are three types of excision surgery for the treatment of acute appendicitis: Single-incision laparoscopic surgery (SILS), conventional laparoscopic appendectomy (CLA) and open appendectomy (OA) (1-4). OA is widely used clinically, even though CLA was first introduced in 1983 (5).

Compared with OA, CLA has the merits of precise diagnosis, minimal trauma, less pain, quick recovery, less bleeding, fewer complications and a reduced duration of hospitalization (6). However, a previous study has reported that CLA has a greater surgical duration than OA, a high cost and provides no significant advantage for the recovery of patients (7).

With the advancement of laparoscopic surgical instruments and technology, SILS was developed and applied for the treatment of acute appendicitis (8). Previous studies have typically compared two methods of appendectomy (9,10), and few have concurrently evaluated the effect of the three surgical methods for acute appendicitis treatment. Therefore, a network meta-analysis was conducted in the present study to systematically assess the therapeutic effect of SILS, CLA and OA in the treatment of acute appendicitis. The aim was to determine the optimal surgical procedure for the treatment of acute appendicitis, and to serve as a reference for surgeons when selecting the appropriate treatment.

## Materials and methods

**Source of data.** PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>) and Embase (<http://www.embase.com>) databases up to April 2016 were systematically searched using the predesigned search terms: 'single-incision laparoscopic appendectomy', 'SILA', 'single incision laparoscopic surgery', 'SILS appendectomy' and/or 'laparoscope or laparoscopic

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**Key words:** single-incision laparoscopic surgery, conventional laparoscopic appendectomy, open appendectomy, acute appendicitis, network meta-analysis

appendectomy' and/or 'open surgery or laparotomy or open appendectomy' and 'appendicite aigue or acute appendicitis'.

**Inclusion and exclusion criteria.** The included studies for analysis had to satisfy the following criteria: i) Studies were randomized controlled trials; ii) at least two of the methods for treatment of acute appendicitis (SILS, CLA and OA) were compared; and iii) the outcome measures included surgical procedure duration, duration of hospital stay, wound infection and incidence of abscesses. All reviews, comments, reports and letters were excluded.

**Data extraction and quality assessment.** The following details of the included studies were extracted independently by two reviewers: The first author, publication year, study region, study time, methods of treatment, the corresponding number of the patients and the demographic characteristics of the participants, including age, gender and body mass index (BMI).

Quality of the included studies was assessed independently by two reviewers in terms of the risk of bias assessment according to Cochrane Collaboration recommendations (11). The discrepancies during the process were discussed with a third reviewer and resolved by consensus.

**Statistical analysis.** All data analyses were performed using ADDIS 1.16.5 software (Drug Information Systems, Groningen, The Netherlands) (12,13). A direct comparison meta-analysis was first performed. Dichotomous data for effectiveness were analyzed using the odds ratio (OR) and 95% confidence interval (CI). Quantitative data for effectiveness were estimated using the standardized mean difference (SMD) and 95% CI. Heterogeneity was evaluated using the  $I^2$  statistical method (14). A value  $>50\%$  was regarded as substantial heterogeneity. A random effects model was applied when significant heterogeneity was identified ( $I^2 >50\%$ ); otherwise, a fixed-effect model was performed (15). In the network meta-analysis, when the three treatments were connected as a loop, the inconsistency was assessed using node-splitting analysis and inconsistency standard deviation (ISD) (16). If node-splitting analysis determined  $P > 0.05$  and the 95% CI of ISD encompassed 1, the consistency model was used for pooled analysis. Otherwise, the inconsistency model was used as described previously (17). Convergence was assessed using potential scale reduction factor (PSRF) and the Brooks-Gelman-Rubin (BGR) method (18), and a value of  $\sim 1$  indicated a good convergence (18).  $P < 0.05$  was considered to indicate a statistically significant result.

## Results

**Study selection.** As shown in Fig. 1, a total of 4,435 records were identified from PubMed (1,620) and Embase (2,815) databases by initial retrieval. Initially, 1,292 duplicate records were removed and another 3,026 studies that deviated from inclusion criteria were excluded by reviewing the titles and abstracts. From the remaining 117 studies, the full-texts were reviewed and 93 studies were removed due to unavailable data or due to the non-randomized control trial design. A total of 24 eligible studies were included in the present meta-analysis (9,10,19-40).

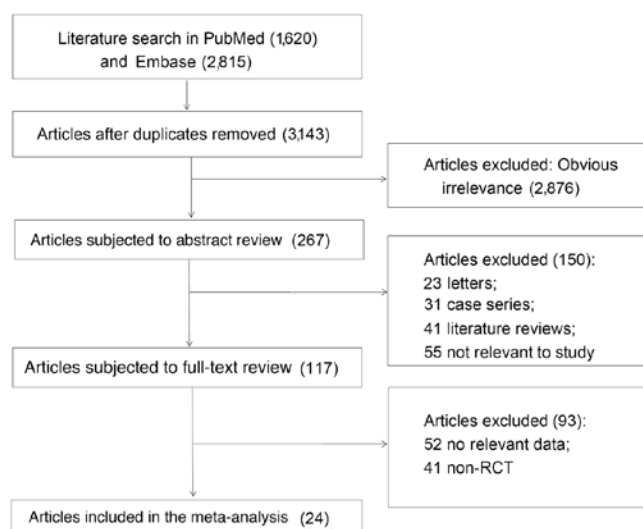


Figure 1. Literature search and study selection. RCT, randomized controlled trial.

**Characteristics of included studies.** The characteristics of the included studies are displayed in Table I (9-32). These include studies published between 1996 and 2015. The participants were distributed in USA, Chile, Turkey, Spain, Sweden, Denmark, Greece, Australia, Korea, India and China. The treatment strategies for acute appendicitis included SILS, CLA and OA. There were no significant differences in demographic characteristics, including age, sex and BMI between the groups in each comparison. Quality assessment showed that there was a relatively low risk of bias in the included studies. However, blinding of participants and personnel (performance bias) and blinding of outcome assessment (detection bias) of the included studies revealed a notably high risk of bias (Fig. 2).

**Results of direct comparison by meta-analysis.** Heterogeneity tests were performed. The appropriate effect model was chosen according to the results of  $I^2$ . As shown in Table II, the random effects model was performed for the three comparisons of surgical procedure duration (CLA vs. OA, CLA vs. SILA and OA vs. SILA) and for the comparison between CLA and OA in duration of hospital stay (all  $I^2 > 50\%$ ), which indicated heterogeneity among studies. Furthermore, duration of hospital stay (CLA vs. SILA and OA vs. SILA), assessment of wound infection and incidence of abscesses were investigated using the fixed-effect model.

**Network analysis.** Parameter setting of ADDIS was follows: Number of chains, 4; tuning iterations, 20,000; simulation iterations, 50,000; thinning interval, 10; inference samples, 10,000; variance scaling factor, 2.5. According to the consistency test, the consistency model was used to pool data regarding to the outcomes of surgical procedure duration ( $P=0.18$ ; ISD, 19.66; 95% CI, 0.70 to 52.27), duration of hospital stay ( $P=0.96$ ; ISD, 1.02; 95% CI, 0.02 to 7.16), wound infection ( $P=0.77$ ; ISD, 0.92; 95% CI, 0.04 to 2.04) and incidence of abscesses ( $P=0.93$ ; ISD, 0.92; 95% CI, 0.04 to 2.04). The PSRFs in each item were 1.02, 1.03, 1.03 and 1.02, which indicated complete convergence. Fig. 3A-D demonstrates the network of surgical procedure duration, duration of hospital stay, wound infection and incidence

Table I. Characteristics of included studies.

Author, year	Study location	Study year	Item	Number of patients	Age (years)	Sex (M/F)	Body mass index	(Refs.)
Park <i>et al.</i> , 2010	Korea	2009	SILS CLA	20 20	NA NA	9/11 8/12	NA NA	(32)
Park <i>et al.</i> , 2012	Korea	2008-2009	SILS CLA	42 62	23.90±11.90 29.90±12.20	14/28 41/21	21.00±2.80 23.00±3.10	(31)
Teoh <i>et al.</i> , 2012	China	2009-2011	SILS CLA	98 97	39.19±15.55 40.65±15.68	58/40 59/38	NA NA	(37)
Lee <i>et al.</i> , 2013	Korea	2010-2011	SILS CLA	116 113	28.40±15.40 28.50±17.20	64/52 68/45	21.40±3.20 22.70±4.40	(10)
Frutos <i>et al.</i> , 2013	Spain	2009-2010	SILS CLA	91 93	28.04±11.03 31.02±12.41	42/49 47/46	23.84±3.98 24.02±3.84	(9)
Kye <i>et al.</i> , 2013	Korea	2009-2010	SILS CLA	51 51	27.55±12.40 29.20±13.98	NA NA	22.03±4.07 21.97±3.49	(27)
Pan <i>et al.</i> , 2013	China	2009-2011	SILS CLA	42 42	34.10±14.50 34.90±14.90	24/18 20/22	23.40±3.50 23.50±4.40	(30)
Mori <i>et al.</i> , 2014	Spain	2011-2012	SILS CLA	60 60	28.10±9.30 30.00±9.20	42/18 34/26	24.60±3.00 24.40±2.10	(29)
Carter <i>et al.</i> , 2014	USA	2010-2012	SILS CLA	37 38	34.00±11.00 35.00±12.00	19/18 24/14	25.00±4.00 25.00±4.00	(17)
Clarke <i>et al.</i> , 2011	USA	1997-2001	CLA OA	23 14	31 (19-60) 33 (18-50)	15/8 9/5	NA NA	(21)
Cox <i>et al.</i> , 1996	Australia	NA	CLA OA	33 31	25 (18-75) 25 (18-84)	33/0 31/0	NA NA	(40)
Ignacio <i>et al.</i> , 2004	USA	2001	CLA OA	26 26	28.4±6.6 27.4±9.3	NA NA	NA NA	(22)
Katkhouda <i>et al.</i> , 2005	USA	NA	CLA OA	113 134	29 (18-71) 28 (17-63)	78/35 104/30	NA NA	(25)
Moberg <i>et al.</i> , 2005	Sweden	2001-2003	CLA OA	81 82	31 (15-71) 31 (15-83)	46/35 58/24	24 (17-34) 25 (17-43)	(28)
Pedersen <i>et al.</i> , 2001	Denmark	NA	CLA OA	282 301	26 (18-40) 27 (18-40)	131/151 143/158	NA NA	(33)
Rieca <i>et al.</i> , 2007	USA	NA	CLA OA	26 26	NA NA	NA NA	≥25 ≥25	(35)
Tzovaras <i>et al.</i> , 2010	Greece	2002-2008	CLA OA	72 75	26 (15-68) 22 (14-65)	NA NA	26 (18-35) 24 (18-36)	(38)
Quezada <i>et al.</i> , 2015	Chile	2003	CLA OA	97 130	39±17.1 38±17.5	49/48 49/81	NA NA	(34)

Table I. Continued.

Author, year	Study location	Study year	Item	Number of patients	Age (years)	Sex (M/F)	Body mass index	(Refs.)
Cipe <i>et al</i> , 2014	Turkey	2012	CLA	121	26.4±9.7	65/56	23.7±2.5	(20)
			OA	120	29.7±12.8	71/49	24.4±2.9	
Jiang <i>et al</i> , 2013	China	2011-2012	SILS	10	32.5± 8.0	10/0	NA	(24)
			CLA	20	34.0± 7.3	13/7	NA	
			OA	20	39.7±13.8	10/10	NA	
Wu <i>et al</i> , 2011	China	2005-2009	CLA	62	75.3±7.1	33/29	NA	(39)
			OA	88	75.5±8.1	46/42	NA	
Kocataş <i>et al</i> , 2013	Turkey	NA	CLA	50	27.4±18.5	NA	NA	(26)
			OA	46	27.4±18.5	NA	NA	
Sozutek <i>et al</i> , 2013	Turkey	2010-2011	SILS	25	30.6±12.4	12/13	23.2±3.79	(36)
			CLA	25	30±11	7/18	23.1±2.58	
			OA	25	32.2±9.4	14/11	23±3.07	
Jategaonkar and Yadav, 2014	India	2009-2011	SILS	212	33.79±12.61	148/64	24.13±2.02	(23)
			CLA	218	35.30±13.37	165/53	23.61±2.40	

Data were expressed as mean ± standard deviation/median (range). SILS, single-incision laparoscopic surgery; CLA, conventional laparoscopic appendectomy; OA, open appendectomy; NA, not applicable.

Table II. Results of direct comparison meta-analysis.

Item	Comparison	K	I <sup>2</sup>	Model	SMD/OR (95%CI)	Z	P-value
Duration of surgical procedure	CLA vs. OA	7	76.1	Random effects model	-0.24 (-0.58 to 0.11)	1.36	0.17
	CLA vs. SILA	12	83.5	Random effects model	0.46 (0.20 to 0.72)	2.61	0.01
	OA vs. SILA	2	96.3	Random effects model	2.44 (-1.33 to 6.72)	1.19	0.23
Duration of hospital stay	CLA vs. OA	11	50.3	Random effects model	0.43 (0.24 to 0.61)	4.56	<0.01
	CLA vs. SILA	10	10.2	Fixed-effect model	-0.10 (-0.21 to 0.00)	1.87	0.06
	OA vs. SILA	2	0	Fixed-effect model	-1.30 (-1.78 to -0.82)	5.31	<0.01
Wound infection	CLA vs. OA	13	0	Fixed-effect model	1.90 (1.18 to 3.07)	2.63	0.01
	CLA vs. SILA	10	0	Fixed-effect model	1.00 (0.55 to 1.81)	<0.01	1
	OA vs. SILA	1	-	-	0.33 (0.04 to 2.99)	1.01	0.31
Incidence of abscesses	CLA vs. OA	9	0	Fixed-effect model	0.60 (0.34 to 1.05)	1.78	0.08
	CLA vs. SILA	6	0	Fixed-effect model	1.79 (0.64 to 5.02)	1.11	0.27

SILS, single-incision laparoscopic surgery; CLA, conventional laparoscopic appendectomy; OA, open appendectomy; SMD, standardized mean difference; OR, odds ratio; CI, confidence interval; K, number of included studies.

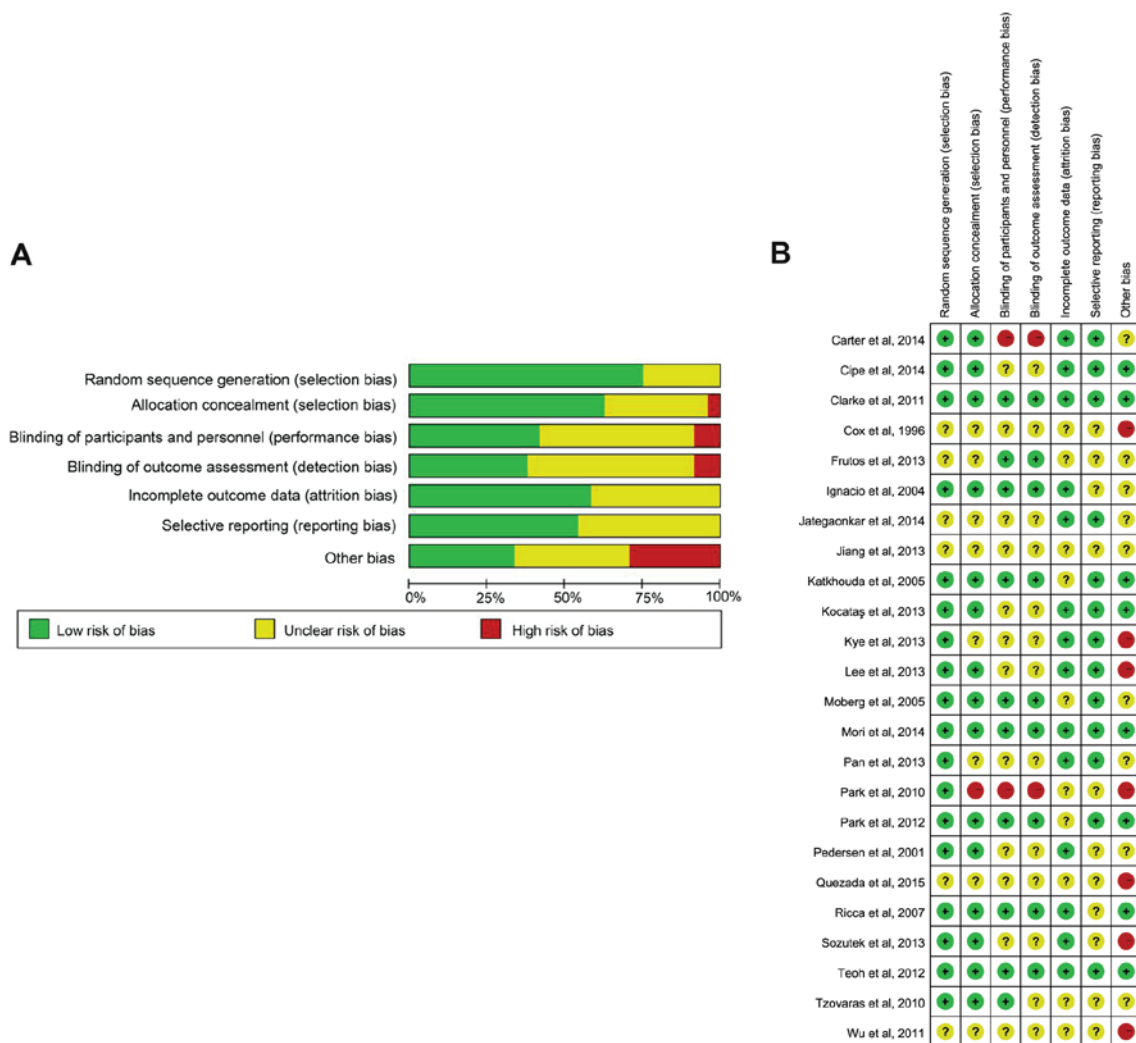


Figure 2. Risk of bias of the included studies. (A) Risk of bias analysis at different levels for all included studies. (B) Distribution of risk of bias analysis at three kinds of levels in each of the included studies. +, low risk; -, high risk; ?, unclear risk.

of abscesses of the three surgical procedures, respectively. As shown in Table III, the pooled results revealed that the surgical

procedure duration of OA was the shortest and a significant difference was identified between OA and SILS (P=0.01).

Table III. Comparison of the different methods for treatment of acute appendicitis.

Factor	Value	Z-value	P-value
Duration of surgical procedure (SMD)			
CLA vs. OA	9.53 (-1.8,21.21)	1.62	0.10
CLA vs. SILS	-9.25 (-17.90, -0.68)	2.11	0.04
OA vs. CLA	-9.53 (-21.21,1.80)	1.62	0.10
OA vs. SILS	-18.72 (-32.29, -5.49)	2.74	0.01
SILS vs. CLA	9.25 (0.68, 17.90)	2.11	0.04
SILS vs. OA	18.72 (5.49, 32.29)	2.74	0.01
Duration of hospital stay (SMD)			
CLA vs. OA	-0.65 (-1.13, -0.39)	3.44	0.01
CLA vs. SILS	0.19 (-0.06, 0.49)	1.34	0.18
OA vs. CLA	0.65 (0.39, 1.13)	3.44	0.01
OA vs. SILS	0.84 (0.53, 1.43)	3.66	0.01
SILS vs. CLA	-0.19 (-0.49, 0.06)	1.35	0.18
SILS vs. OA	-0.84 (-1.43, -0.53)	3.66	0.01
Wound infection (OR)			
CLA vs. OA	0.43 (0.24, 0.75)	2.90	0.01
CLA vs. SILS	1.23 (0.63, 2.39)	0.61	0.54
OA vs. CLA	2.31 (1.33, 4.10)	2.90	0.01
OA vs. SILS	2.83 (1.20, 6.76)	2.36	0.02
SILS vs. CLA	0.81 (0.42, 1.58)	0.61	0.54
SILS vs. OA	0.35 (0.15, 0.83)	2.36	0.02
Incidence of abscesses (OR)			
CLA vs. OA	1.73 (0.79, 3.88)	1.35	0.18
CLA vs. SILS	0.38 (0.10, 1.19)	1.53	0.13
OA vs. CLA	0.58 (0.26, 1.26)	1.35	0.18
OA vs. SILS	0.22 (0.04, 0.89)	2.01	0.04
SILS vs. CLA	2.63 (0.84, 10.34)	1.53	0.13
SILS vs. OA	4.54 (1.12, 23.51)	2.01	0.04

SILS, single-incision laparoscopic surgery; CLA, conventional laparoscopic appendectomy; OA, open appendectomy; SMD, standardized mean difference; OR, odds ratio.

However, there was no significant difference in surgical duration between SILS and CLA. In comparison with OA, SILS and CLA exhibited a significantly shorter duration of hospital stay (all  $P < 0.01$ ) and lower risk of wound infection (SILS vs. OA,  $P = 0.02$  and CLA vs. OA,  $P < 0.01$ , respectively); however, no significant differences were indicated between SILS and CLA. Furthermore, SILS exhibited a significantly lower incidence of abscesses compared with OA ( $P = 0.04$ ), while no significant difference was observed between OA and CLA.

Ranking of the three methods for treatment of acute appendicitis is displayed in Fig. 4. Regarding surgical procedure duration, OA was ranked the optimal method whereas SILS was ranked as the worst. However, regarding duration of hospital stay, wound infection and incidence of abscesses, SILS was ranked as the optimal method whereas OA was ranked as the worst.

## Discussion

In the present study, the outcomes of three appendectomy methods were systematically compared using network

meta-analysis. The results indicated that SILS resulted in a shorter duration of hospital stay, lower incidence of wound infection and lower incidence of abscesses, but demonstrated a longer surgical procedure duration compared with OA. However, no significant differences were identified between CLA and SILS in any outcome.

The present results were in accordance with previous meta-analyses (6,41), which showed that laparoscopic appendectomy acquired faster postoperative rehabilitation, shorter hospital stay and fewer postoperative complications compared with OA. However, laparoscopic appendectomy exhibited a longer surgical procedure duration compared with OA. It may be suggested that the application of laparoscopic equipment increases the complexity of the surgery and requires improved surgical skill; thus, the surgical procedure duration was prolonged. However, improvements in surgical skill may reduce the surgical time. Furthermore, the small wounds created during CLA and SILS restrict the range of movement during surgery, which may prolong the duration of the surgical procedure.



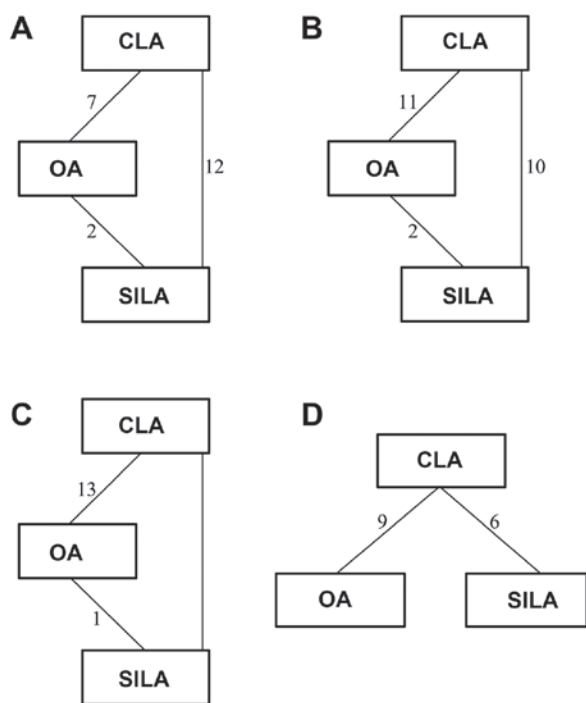


Figure 3. Network of the treatments for acute appendicitis regarding (A) surgical procedure duration, (B) duration of hospital stay, (C) wound infection and (D) incidence of abscesses. The numbers placed over the connecting lines indicate the number of related studies between two surgical procedures. SILS, single-incision laparoscopic surgery; CLA, conventional laparoscopic appendectomy; OA, open appendectomy.

Ranks	Best	Worst	
Surgical procedure duration	OA	CLA	SILS
Duration of hospital stay	SILS	CLA	OA
Wound infection	SILS	CLA	OA
Incidence of abscesses	SILS	CLA	OA

Figure 4. Ranking of the treatments in terms of operative time, length of hospital stay, wound infection and abscesses. SILS, single-incision laparoscopic surgery; CLA, conventional laparoscopic appendectomy; OA, open appendectomy.

Although SILS and CLA do not reduce surgical procedure duration in comparison with other procedures, CLA and SILS are used widely in the clinic due to their associated benefits. For example, laparoscopic surgery may be used to comprehensively and precisely check lesions in enterocoelia (42). Furthermore, in some cases, such as with obese patients, a larger wound is required to excise the appendix when OA is performed (43). Additionally, single-incision laparoscopic appendectomy (SILA) and CLA are postulated to reduce postoperative pain and enhance cosmesis effectively (44). It is likely that CLA and SILS result in reduced pain due the smaller wound that is cut.

SILS is an improved method of laparoscopic appendectomy developed from CLA (9) and is valuable for use in clinical settings due to the smaller scar it leaves compared with CLA. Saber *et al* (45) simplified SILS in clinical settings and improved the surgical procedure. Furthermore,

Hua *et al* (46) demonstrated that SILA is a feasible and safe alternative procedure to CLA. Additionally, OA, CLA and SILA are all effective for appendicitis; however, SILA is considered a minimally invasive surgery (47), and has developed during the evolution of the appendectomy procedure from OA to CLA to SILA. It may be possible for surgeons improve their skills to reduce the duration of surgery and gain improved surgical success. The future prospects of SILS are better than those of OA and CLA due to patients' requests to undergo a minimally scarring and painless procedure with a good prognosis. Therefore, SILS procedures should be developed and simplified according to clinical experience in order to reduce the duration of the surgical procedure and abscess risk.

Heterogeneity was observed in the present study. The potential causes and sources of heterogeneity are diverse. In the present study, articles from different regions, including USA, Turkey, Australia, South Korea, Spain, India and China were included. The patient characteristics, surgical skills, surgical practice and severity of appendicitis may contribute to the heterogeneity, in addition to the sample size of each study. Furthermore, a few shortcomings should be taken into account in this network meta-analysis. Firstly, the effectiveness among all of the treatments for acute appendicitis was not compared due to the incompleteness of data. A study by Wilms *et al* (48) compared the outcomes between conservative antibiotics and appendectomies, but did not classify the exact surgical approaches (CLA or OA). Therefore, the outcomes of antibiotics were not included. For further studies, this point should be considered and a strict experimental design followed. Additionally, in the network meta-analysis of the incidence of abscesses, the loop was not closed as OA and SILA were not compared in any of the included studies; therefore, it was not possible to use node-splitting analysis for consistency testing. Furthermore, ADDIS software is not freely programmable, and thus the results that can be reported were limited. Another potential limitation was that only four outcomes were considered in the present network meta-analysis and alternative outcomes such as pain score, amount of bleeding and other postoperative complications were not included due to a lack of original data. Furthermore, only two studies that compared OA and SILS were included in the present study, which may limit the credibility of the present results. Further studies and stricter experimental design are required to further support the present results. Despite these limitations, there are several strengths in the present meta-analysis. The three methods of managing acute appendicitis were systemically and comprehensively compared for the first time. The results of the present study may provide guidance for the treatment of acute appendicitis in the clinic.

In conclusion, the present comprehensive network meta-analysis indicates that laparoscopic appendectomy, particularly SILS and CLA has greater advantages for treating acute appendicitis compared with OA. Considering patients' requests for minimal scarring and for the procedure to be painless with a good prognosis, SILS appears to be an optimal procedure choice. However, SILS requires improvement and simplification to reduce the duration of the surgical procedure.

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