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Acute appendicitis can be treated with single incision laparoscopy: a systematic review of randomized controlled trials.

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Abstract

Aim

Single-incision laparoscopic surgery (SILS) has been proposed as the next step in minimally invasive surgery for appendicectomy. Previous reviews have summarized the results of low-evidence comparative studies, suggesting that the two approaches are comparable in terms of outcomes but showing the need for randomized controlled trials (RCTs). This review offers a meta-analyses of RCTs on this topic to evaluate the safety and efficacy of single-incision laparoscopic appendectomy (SILA).

Method

A comprehensive research of electronic databases was performed. Primary outcomes (overall and access-specific morbidity) were designated as safety issues. Secondary outcomes were pain, cosmesis, operative time, conversion rate and length of hospital stay.

Results

After exclusions, five RCTs satisfied the inclusion criteria. They included a total of 761 patients [379 SILA and 382 conventional three-port laparoscopic appendectomies (CLA)]. No significant differences were found in overall morbidity, early wound morbidity or length of stay between SILA and CLA. Cosmesis and pain were not comparable due to different scales and time records. Conclusions on the incisional hernia rate were not reliable due to short follow-up periods.

Conclusion

SILA can be considered an acceptable alternative to CLA in the treatment of acute appendicitis, but an economic evaluation of the various techniques for single access must be performed before its widespread clinical introduction. Better-designed RCTs are necessary to define a population in which SILA could have major benefits.

Keywords:

- Appendicitis; laparoscopy; single site surgery

What does this paper add to the literature?

This is the first systematic review to compare single-incision laparoscopic appendectomy with conventional three-port laparoscopic appendectomy in the adult population, done exclusively with RCTs and following the Cochrane methodology. It thus adds significant value to evidence-based practice in the surgical treatment of the very common disease of acute appendicitis.

Introduction

Background

Single-port surgery may be the next step in minimally invasive surgery after conventional laparoscopy [1]. Numerous case series of single-incision laparoscopic appendectomy (SILA) have been published since 2009 [2]. However, studies with higher-level evidence have only been reported recently. Compared with conventional laparoscopic appendectomy (CLA), commonly performed with a three-port technique, SILA performed through the umbilicus may improve cosmesis, reduce post-operative pain and hospital stay, and lead to a quicker return to work and a quality of life in general [3]. The potential drawbacks of SILA include the loss of triangulation, impaired view, instrument conflicts outside the abdomen and the cost of the devices [4].

Aim

The aim of this review was to meta-analyse data from randomized controlled trials (RCTs) reporting on the effectiveness and safety of SILA.

Method

Study design and participants

This review was conducted in accordance with the guidelines of the Quality of Reporting of Meta-analysis (QUORUM) statement [5] and Cochrane Handbook for Systematic Reviews of Interventions [6].

We selected all RCTs comparing SILA (irrespective of the type of multiport devices used) with CLA. Inclusion criteria were patients undergoing surgery for appendicitis in pre-adolescent, adolescent or adult age categories (i.e. more than 11 years old).

Systematic literature search

Two authors performed an online literature search on MEDLINE, Embase, the Cochrane Central Register of Controlled Trials and Cochrane Library databases. The following medical subject heading (MeSH) terms and free words were used in all possible combinations: ‘single incision’, ‘single site’, ‘single port’, ‘single access’, ‘transumbilical’, ‘laparoscopic appendectomy’, ‘laparoscopic appendicectomy’. The PubMed string for search strategy is reported in full as Supporting Information. The ‘related article’ function was used to expand the search and other titles were manually extracted from the references and from a free-word electronic search of the Google Scholar database. No language restriction was made. Two independent reviewers subsequently selected from the title and abstract those articles to be viewed in full-text; a third reviewer was questioned in case of disagreement. Where articles from the same centre were published with

overlapping dates of patient recruitment or in cases of 'salami' publications [7], the most recent or highest-quality article was chosen.

Primary and secondary outcomes

The primary outcomes studied were overall and abdominal wall-specific morbidity. Analysis of data on pain, cosmesis, operative time, length of hospital stay and conversion were defined as secondary outcomes.

Data extraction

A meta-analysis of the data was conducted following the procedures described in the Cochrane Handbook for Systematic Reviews of Interventions [6] using RevMan5 and mix 2.0. The risk ratio was calculated to compare the following outcomes: overall morbidity, operative time and conversion rate to laparotomy. Mean difference was compared for operative time and postoperative stay.

Data synthesis

All outcomes were synthesized using a random effects (M–H) model. While there is debate on the conditions under which fixed versus random effects models are most appropriate, we chose to uniformly use a random effects model because of the arguments put forth by Ades and Higgins [8], DerSimonian and Laird [9] and Fleiss and Gross [10] on the suitability of using random effects in medical decision-making contexts. In addition, Shuster *et al*. [11] found that random effects models are preferable in the case of rare events, as we have here. The degree of heterogeneity between studies was assessed using τ^2, χ^2 (Cochran's Q) and I^2. We considered values of $\tau^2 > 1.00$ and χ^2 values with associated P-values < 0.01, with I^2 values > 0.50 being used as indicators of heterogeneity. In terms of sensitivity analysis, we ran both fixed and random effects models to compare results and examined weighting sensitivity plots. We also examined heterogeneity plots, exclusion sensitivity plots and dissemination sensitivity plots to assess the risk of publication bias.

Results

Description of included and excluded studies

From a systematic search of the literature we initially selected 185 studies. After the exclusion of articles based on the age of the participants and veterinary articles 106 remained. After reading the titles, 53 articles were aligned with the aim of our review and 38 were extracted in full text after the abstracts were analysed. Of those, five articles met the inclusion criteria [12-16], while 33 were excluded (Fig. 1). The characteristics of the included trials are summarized in Table 1. The trials were conducted between 2009 and 2011 and published in 2012 or 2013 and only one was a multicentre study. There were 761 patients pooled for analysis, 379 who underwent SILA and 382 who underwent CLA. All studies reported having done sample size calculations through power analysis. Only Frutos *et al*. [16] and Kye *et al*. [13] reported body mass index. Duration of follow-up was between 14 and 30 days. Three studies reported on surgical experience but definitions differed [12, 14, 16]. The exclusion criteria differed between all the included studies: Frutos *et al*. [16] and Teoh *et al*. [12] excluded abscess and/or local or diffused peritonitis, Lee *et al*. [14] excluded abscess only and Sozutek *et al*. [15] did not specify any exclusion criteria. The rate of complicated appendicitis, although different between studies, was comparable between arms. Technical details of the surgical procedures are described in Table 2. The mesoappendix division and the transection of the base of the appendix were performed with variety of techniques and

instruments. Also, the types of monoports and instruments (angulated, reticulated or straight) used for SILA were different. Despite these differences between studies, every single trial used a homogeneous technique in both the conventional and three-port groups.

Table 1. Clinical characteristics of the patients included in the selected trials

References	No. of patients		Age (years)	Severity of appendicitis (no. of patients)	Local exclusion criteria	Experience of surgical team	Primary outcomes	Follow-up
	Single access	Three-port access						
Frutos *et al*. [16]	91	93	> 11	Acute (26), phlegmonous (39), purulent (93), gangrenous (26)	Clinical or radiological suspicion of abscess or peritonitis	Experience in advanced laparoscopy and training in SILA	Morbidity	14 days
Lee *et al*. [14]	116	113	> 16	NR	CT or ultrasound positive for abscess	Extensive experience with CLA, > 10 SILA	Morbidity	14 days
Teoh *et al*. [12]	98	97	18–75	Normal (7), acute (101), perforated (30), gangrenous (37), abscess (20)	Generalized peritonitis or abscess/abdominal mass	Performed or supervised by surgeons with experience > 20 SILA and > 100 advanced laparoscopies	Pain	14 days
Sozutek *et al*. [15]	25	25	> 18	Acute (30), phlegmonous (10), perforated (10)	NR	NR	Pain	30 days
Kye *et al*. [13]	51	51	NR	Acute (86), perforated (16)	NR	NR	Pain	20 months

1. NR, not recorded; SILA, single-incision laparoscopic appendectomy; CLA, conventional three-port laparoscopic appendectomy.

Table 2. Technical details of the procedures for single-incision laparoscopic appendectomy (SILA) and conventional three-port laparoscopic appendectomy (CLA)

References	SILA trocar [skin incision length]	Type of instrument for SILA	CLA ports	Stump sealing (CLA and SILA)	Mesoappendix division (CLA and SILA)
Frutos *et al*. [16]	SILS port (Covidien, Mansfield, Massachusetts, USA) [20 mm]	Dedicated	11 mm umbilical 12 mm left lower quadrant 5 mm right upper quadrant	Endostapler	Endoloop
Lee *et al*. [14]	Octoport (Dalim, Seoul, Korea) [15 mm]	Conventional	10 mm umbilical 5 mm suprapubic 5 mm left lower quadrant	Endoloop	Ultrasonic shears
Teoh *et al*. [12]	Multiple fascial insertion (two 5-mm ports and one 10-mm port) [13 mm]	Dedicated and conventional	10 mm umbilical 5 mm right lower quadrant 5 mm left lower quadrant	Endoloop	Ultrasonic shears
Sozutek *et al*. [15]	SILS Port (Covidien, Mansfield, Massachusetts, USA) [20 mm]	NR	10 mm umbilical 5 mm right lower quadrant 5 mm suprapubic	Endoloop	Bipolar energy device
Kye *et al*. [13]	Home made glove-port [20 mm]	Conventional	10 mm umbilical 5 mm suprapubic 5 mm left lower quadrant	Endoloop	Ultrasonic shears

1. SILS, single-incision laparoscopic surgery; NR, not recorded.

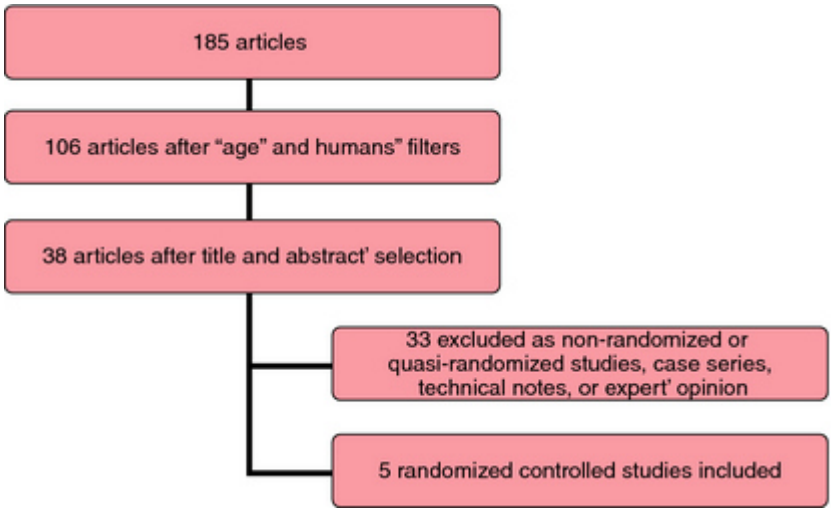

Figure 1. Literature search results and selection of studies.

Quality assessment of included studies

Evaluation of methodological quality of the included trials was performed with the modified Jadad score [17]; all studies were of good quality Fig. 2). Appropriate randomization and allocation concealment were performed in all trials. Only Lee *et al*. [14] reported the use of modified intention to treat and only Teoh *et al*. [12] blinded the patient and outcome assessor.

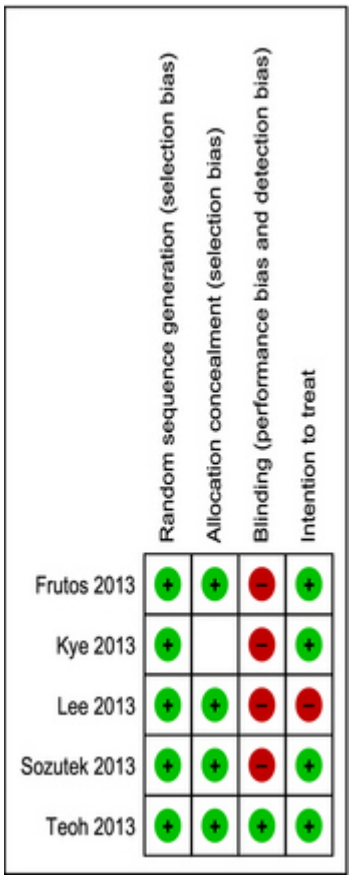

Figure 2. Table of bias assessment risk.

Sensitivity analysis for the binary outcomes (i.e. overall morbidity, complication rate and conversion rate) showed negligible differences between the results from random and fixed effects models; visual analysis of a weighting sensitivity plot also verified this result. Analysis of heterogeneity and exclusion selectivity plots indicated that none of studies included on these outcomes were outliers. Finally, an analysis of dissemination selectivity plots did not indicate publication bias for any of the binary outcomes.

Primary and secondary outcomes

There was no statistically significant difference in overall morbidity [10.2% in the single-incision group versus 9.4% in the conventional three-port group; risk ratio (RR) = 1.06, 95% CI 0.69–1.62, $P = 0.80$] (Fig. 3). The postoperative abdominal wall complication rate (defined as wound infection, bleeding, hernia or eventration) was lower in the single-incision group (4.9% *vs* 5.9%) but was not statistically significant (RR = 0.87, 95% CI 0.47–1.60, $P = 0.65$) (Fig. 4).

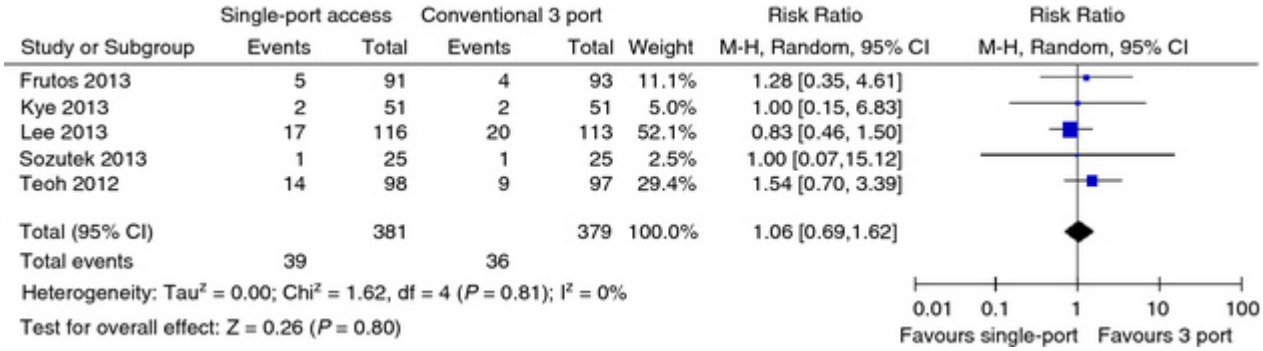

Figure 3. Meta-analysis of overall morbidity outcome.

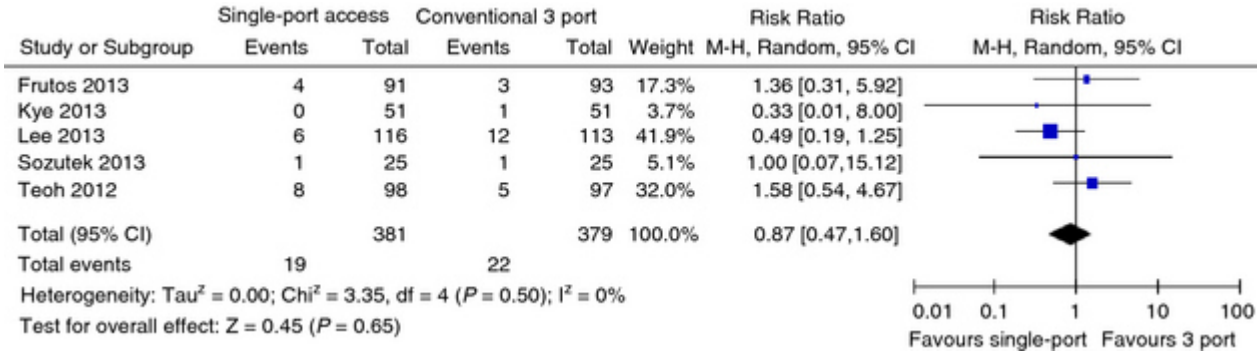

Figure 4. Meta-analysis of post-operative abdominal wall complication rate.

All five trials reported on the postoperative pain outcome, but we did not synthesize the results because different scales and evaluation times were used in each (Table 3). Frutos *et al.* [16] and Kye *et al.* [13] reported statistically significant lower postoperative pain in the single-incision group ($P < 0.00$ and $P = 0.01$, respectively); however, Teoh *et al.* [12], Sozutek *et al.* [15] and Lee *et al.* [14] did not report statistically significant differences in the overall pain scores.

Table 3. Comparison between different scales of postoperative pain

Study	Scale	Evaluation after surgery	Laparoscopic appendectomy (mean ± SD)		
			CLA	SILA	*P*
Frutos *et al*. 2013 [16]	VAS (graded from 0 to 10)	At 9 and 12 h	3.78 ± 1.76	2.76 ± 1.64	< 0.001
Teoh *et al*. 2012 [12]	VAS (graded from 0 to 100)	At 24 h	NR		0.253
Sozutek *et al*. 2013 [15]	VAS (graded from 0 to 10)	At 3 h	5.1 ± 1.2	4.4 ± 1.1	0.001
		At 6 h	3.4 ± 1.0	2.9 ± 0.86	0.001
		At 12 h	2.1 ± 0.81	2.1 ± 0.97	0.001
		At 24 h	2.0 ± 1.0	2.0 ± 0.95	0.001
Lee *et al*. 2013 [14]	VAS (value NR)	At 12 h	NR		0.651
		At 24 h			0.555
		At 36 h			0.570
		At 14 days			0.631
Kye *et al*. 2013 [13]	VAS (value NR)	At 24 h	3.22 ± 1.22	3.22 ± 1.22	0.012
		At 48 h	2.20 ± 1.03	2.04 ± 1.12	0.460

1. VAS, visual analogue scale; NR, not reported; CLA, conventional three-port laparoscopic appendectomy; SILA, single incision laparoscopic appendectomy.

Only two trials reported on postoperative cosmesis, but meta-analysis was not performed because a different scale was used in each (Table 4). Teoh *et al*. [12] reported statistically significantly better wound cosmesis in the single-incision group ($P < 0.00$), while Lee *et al*. [14] did not report a statistically significant difference in postoperative cosmesis ($P = 0.13$).

Table 4. Comparison between different scales of postoperative cosmesis

Study	Scale of cosmesis score	Evaluation	Laparoscopic appendectomy (mean ± SD)		
			CLA	SILA	*P*
Frutos *et al*. 2013 [16]	NR				
Teoh *et al*. 2012 [12]	Rating from 0 to 100	At 2 weeks	82.50 ± 0.17	73.43 ± 24.09	0.002

1. NR, not recorded; CLA, conventional three-port laparoscopic appendectomy; SILA, single incision laparoscopic appendectomy.

Table 4. Comparison between different scales of postoperative cosmesis

Study	Scale of cosmesis score	Evaluation	Laparoscopic appendectomy (mean ± SD)		
			CLA	SILA	*P*
Sozutek *et al*. 2013 [15]	NR				
Lee *et al*. 2013 [14]	Rating from 0 to 10	At first month	6.7 ± 0.8	7.2 ± 0.8	0.247
Kye *et al*. 2013 [13]	NR				

The length of hospital stay, measured as postoperative hours, was only reported by Frutos *et al*. [16] and there were no statistically significant differences in the two groups ($P = 0.12$); similar results have emerged from the analysis of length of stay, measured as postoperative days (mean difference = −0.45, 95% CI −1.76 to 0.86, $P = 0.50$) (Fig. 5). However, the study by Kye *et al*. [13] reported a reduction in length of stay of 1.75 days in the SILA group. If the results of Kye *et al*. are excluded from the meta-analysis, the postoperative day measure was 13/100th of a day less with the conventional three-port procedure; however, the difference was still not statistically significant.

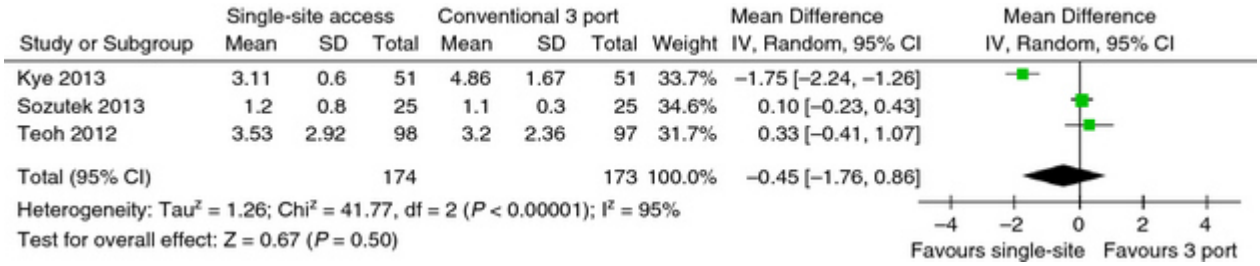

Figure 5. Meta-analysis of operative time.

In terms of operative time, there was much heterogeneity between studies ($I^2 = 81\%$) and a sensitivity analysis suggested some evidence for dissemination bias. When not adjusting for that bias, operative times were 1.98 min shorter under the conventional three-port procedure, but the difference was not statistically significant (mean difference = 1.98, 95% CI −3.40 to 7.36, $P = 0.47$) (Fig. 6). However, a visual analysis of dissemination selectivity plots and the nonstatistically significant results of Begg's rank correlation test and Egger's regression test indicated a small degree of publication bias. Therefore, a trim-and-fill algorithm was used to reduce the amount of study bias. The results of the trim-and-fill algorithm indicated that the bias-adjusted mean difference in operative times (in favour of the conventional three-port procedure) was statistically significant (mean difference = 4.79, 95% CI 2.75– 6.83; Fig. 6). When adjusting for that bias, the operative time was 4.79 min shorter under the conventional three-port procedure and the difference was statistically significant (95% CI 2.75–6.83). In either case, operative times were slightly shorter using the conventional three-port procedure.

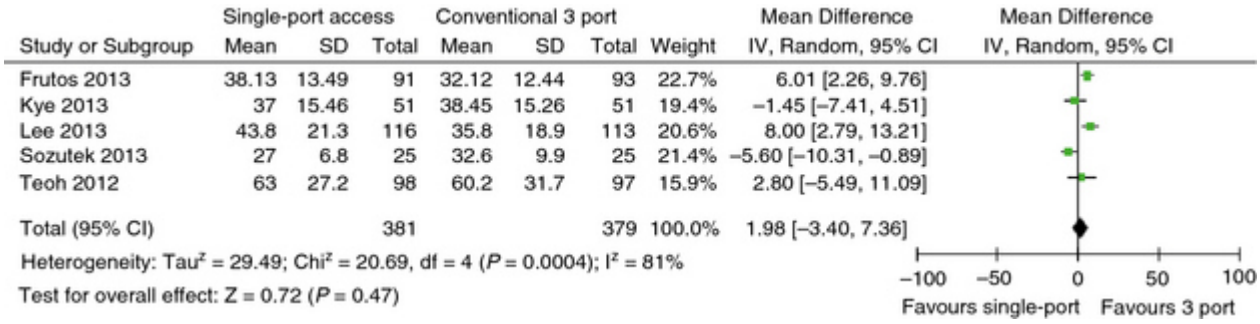

Figure 6. Meta-analysis of length of hospital stay.

The conversion to open surgery rate was lower in the conventional three-port group (2.3% *vs* 1%), but this was not statistically significant (OR = 2.29, 95% CI 0.68–7.78, $P = 0.18$) and the RR was 2.21 (95% CI 0.68–7.14) (Fig. 7).

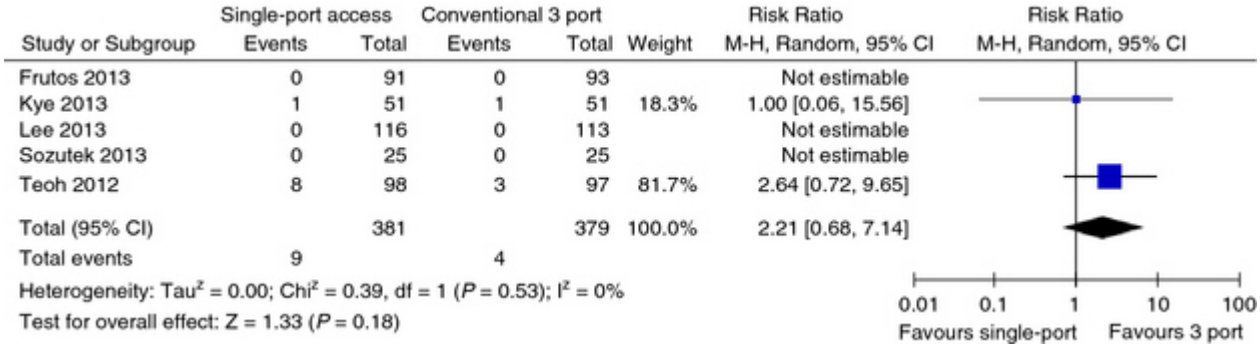

Figure 7. Meta-analysis of laparotomic conversion rate.

Discussion

Clinical evidence and consensus development conferences recommend that laparoscopic appendicectomy is limited to premenopausal women; its application in complicated appendicitis is still debated [18]. Previous clinical studies that have examined the role of SILA are potentially biased by the absence of randomization, consequently whether or not SILA is an inferior method has not definitely been ascertained [19]. This review, which has pooled the results of recently reported RCTs, has shown that SILA is at least comparable to CLA in the treatment of acute appendicitis and may have some benefits.

The five RCTs pooled in this study were all published in 2012 or 2013, with patients receiving surgery between 2009 and 2011. The data in this study therefore probably include patients on surgeons' learning curves [20] and this might influence results, as shown in previous studies concerning single port-cholecystectomy [21]. There is a paucity of literature examining the learning curve for SILA. Only a paediatric series has analysed skills issues and prescribed a minimum of five cases to demonstrate mastery of the technique [22]. In the studies included in our review the specification of previous training in SILA was only quantified only by Teoh *et al*. [12] and by Lee *et al*. [14], which considered at least 20 and 10 SILA procedures, respectively, as necessary to ensure competence in SILA. Frutos *et al*. [16] described 'previous training in SILA' without further specification.

Primary outcomes

In this analysis pooled data concerning overall morbidity did not show any statistically significant difference between SILA and CLA and abdominal wall morbidity was equally insignificant. When looking at the data using the Dindo–Clavien classification of surgical morbidity [23], only one patient required reoperation (this patient was in the CLA group). This patient required reoperation for a postoperative haemoperitoneum from an injury to an epigastric vessel.

Secondary outcomes

Data on pain have not been synthesized due to the heterogeneity of scales and recording time. Although biased by the above considerations, neither a better outcome in terms of postoperative pain nor a reduction in the need for analgesics was evidenced from the RCTs.

The results of this analysis showed that operative time, as seen in most single-incision surgery [24], slightly increases for SILA even if the mean difference does not exceed 5 min. Therefore, the advantages of SILA could be related only to cosmesis; however, in our analysis the data were not homogeneous and we could not pool them together in a forest plot. In fact, cosmesis is a difficult outcome to compare as it results from a subjective judgement (which was examined in the included studies with the exception of Kye *et al*. [13]); a more reliable objective determination of the real aesthetic result could be made from a visualization and judgement of the scar made after 3–6 months by an external expert assessor (i.e. a plastic surgeon) as has been included in the ongoing MUSIC study (MUltiport *vs* SIngle port Cholecystectomy) [25]. Quality of life was only studied adequately in two trials [12, 14]; in the first with a GIQLI (Gastrointestinal Quality of Life Index) test and in the second with the SF-36 (Medical Outcomes Study 36-Item Short-Form Health Survey) questionnaire. The other three studies measured only the 'return to normal activity' intended as return to work or everyday physical activity. In all cases, however, no important differences were found in the two groups.

Financial cost was not compared in the studies included in our met-analysis. It has been reported that SILA can be performed safely with the same instruments and costs as CLA [26]. In this study, high-energy dissection instruments (which have not proved necessary for appendectomy) [27], dedicated angulated instruments and commercial devices for the single-access port have been widely used and they have a cost that might influence healthcare advisors in the choice between two equivalent operations. The use of conventional instruments, bipolar coagulation for the mesoappendix and limited application of the endostapler for the transection of the stump (only in those cases of gangrene of the basis) would significantly lower the cost of the operation. Moreover, the solution suggested by Tai *et al*. [28] and adopted in the trial by Kye *et al*. [13] considers the use of the a 'home-made' glove-port, which would not influence the budget, unlike commercial single-site ports.

Patient selection

The use of additional ports is, as expected, significantly higher in SILA and has proven necessary in 1–10% of the cases. This is probably due to an unselected population of patients in at least three of the five studies examined (Table 1), which identified a similar rate of complicated appendicitis (abscess, gangrene, perforation, peritonitis) in both groups (SILA and CLA) to that described in the literature [29]. We believe that this subgroup may have partially changed the real outcomes of SILA negatively. It is possible that patient selection (which can be performed preoperatively or after laparoscopic exploration) that excludes patients affected by complicated appendicitis could enhance the benefits of SILA [30].

Conclusions and implications for practice and further research

The surgical community is divided between enthusiasm and scepticism about single-access surgery. The failure of our analyses to show any significant differences in the main outcomes between SILA and CLA justifies further trials and clinical application of the technique in selected patients. One limitation of this study is the short follow-up of patients within the studies examined, with the majority having a follow-up of less than a month (in only one study did follow-up exceed a year [13]), which is sufficient for immediate complications (haemorrhage or infection) but inadequate to determine differences in incisional hernias, which is one of the main issues that arises in single-site surgery [31]. To confidently compare cosmesis and quality of life, well-constructed randomized trials to ascertain the superiority of the single access method and the effect are needed. These would probably be enhanced by the selection of patients for SILA who may benefit most from these improvements (i.e. uncomplicated appendicitis, fertile women, the employed and young patients). A multicentre trial called AMUSING (Appendectomy Multiport vs. SINGle port) registered at www.clinicaltrials.gov, the US International Clinical Trials Databank (US National Institutes of Health, PRS 10/31/2012, protocol number NCT01720082), is currently recruiting and has been constructed for a selected group of patients in order to answer these questions.

References

- 1 *Cuschieri A. Single-incision laparoscopic surgery. J Minim Access Surg 2011; 7: 3–5.*
- 2 *Rehman H, Rao AM, Ahmed I. Single incision versus conventional multi-incision appendicectomy for suspected appendicitis. Cochrane Database Syst Rev 2011; (7): CD009022.*
- 3 *Greaves N, Nicholson J. Single incision laparoscopic surgery in general surgery: a review. Ann R Coll Surg Engl 2011; 93: 437–40.*
- 4 *Mynster T, Wille-Jørgensen P. Single incision laparoscopic surgery: new 'toys for boys'? Colorectal Dis 2011; 13: 351.*
- 5*Moher D, Cook DJ, Eastwood S et al. Improving the quality of reports of meta-analyses of randomised controlled trials: the QUOROM statement, QUOROM Group. Br J Surg 2000; 87: 1448–54.*
- 6*Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions, version 5.0.2. http://www.cochrane-handbook.org. The Cochrane Collaboration. 2009 (accessed March 2013).*
- 7*Abraham P. Duplicate and salami publications. J Postgrad Med 2000; 46: 67–9.*
- 8*Ades AE, Higgins JPT. The interpretation of random-effects meta-analysis in decision models. Med Decis Making 2005; 25: 646–54.*
- 9*DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986; 7: 177–88.*
- 10 *Fleiss JL, Gross AJ. Meta-analysis in epidemiology, with special reference to studies of the association between exposure to environmental tobacco smoke and lung cancer: a critique. J Clin Epidemiol 1991; 44: 127–39.*
- 11 *Shuster JJ, Jones LS, Salmon DA. Fixed vs random effects meta-analysis in rare event studies: the rosiglitazone link with myocardial infarction and cardiac death. Stat Med 2007; 26: 4375–85.*
- 12 *Teoh AY, Chiu PW, Wong TC et al. A double-blinded randomized controlled trial of laparoendoscopic single-site access versus conventional 3-port appendectomy. Ann Surg 2012; 256: 909–14.*
- 13 *Kye BH, Lee J, Kim W et al. Comparative Study between single-incision and three-port laparoscopic appendectomy: a prospective randomized trial. J Laparoendosc Adv Surg Tech A 2013; J Laparoendosc Adv Surg Tech A. 23: 431–6.*

- 14 *Lee WS, Choi ST, Lee JN et al. Single-port laparoscopic appendectomy versus conventional laparoscopic appendectomy: a prospective randomized controlled study. Ann Surg 2013; 257: 214–8.*
- 15 *Sozutek A, Colak T, Dirlik M et al. A prospective randomized comparison of single-port laparoscopic procedure with open and standard 3-port laparoscopic procedures in the treatment of acute appendicitis. Surg Laparosc Endosc Percutan Tech 2013; 23: 74–8.*
- 16 *Frutos MD, Abrisqueta J, Lujan J et al. Randomized prospective study to compare laparoscopic appendectomy versus umbilical single-incision appendectomy. Ann Surg 2013; 257: 413–8.*
- 17 *Jadad AR, Moore RA, Carroll D et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials 1996; 17: 1–12.*
- 18 *Agresta F, Ansaloni L, Baiocchi GL et al. Laparoscopic approach to acute abdomen from the Consensus Development Conference of the Società Italiana di Chirurgia Endoscopica e nuove tecnologie (SICE), Associazione Chirurghi Ospedalieri Italiani (ACOI), Società Italiana di Chirurgia (SIC), Società Italiana di Chirurgia d'Urgenza e del Trauma (SICUT), Società Italiana di Chirurgia nell'Ospedalità Privata (SICOP), and the European Association for Endoscopic Surgery (EAES). Surg Endosc 2012; 26: 2134–64.*
- 19 *Gill RS, Shi X, Al-Adra DP et al. Single-incision appendectomy is comparable to conventional laparoscopic appendectomy: a systematic review and pooled analysis. Surg Laparosc Endosc Percutan Tech 2012; 22: 319–27.*
- 20 *Frutos MD, Abrisqueta J, Luján JA et al. Single incision transumbilical laparoscopic appendectomy: initial experience. Cir Esp 2011; 89: 37–41.*
- 21 *Joseph M, Phillips MR, Farrell TM et al. Single incision laparoscopic cholecystectomy is associated with a higher bile duct injury rate: a review and a word of caution. Ann Surg 2012; 256: 1–6.*
- 22 *Burjonrappa SC, Nerkar H. Teaching single-incision laparoscopic appendectomy in pediatric patients. JSLS 2012; 16: 619–22.*
- 23 *Dindo D, Demartines N, Clavien PA. Classification of surgical complications. A new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004; 240: 205–13.*
- 24 *Trastulli S, Cirocchi R, Desiderio J et al. Systematic review and meta-analysis of randomized clinical trials comparing single-incision versus conventional laparoscopic cholecystectomy. Br J Surg 2013; 100: 191–208.*
- 25 *Arezzo A, Morino M. Endoscopic surgery through single-port incision: time for a trial? Surg Endosc 2011; 25: 1709–11.*
- 26 *Chiu CG, Nguyen NH, Bloom SW. Single-incision laparoscopic appendectomy using conventional instruments: an initial experience using a novel technique. Surg Endosc 2011; 25: 1153–9.*
- 27 *Vettoretto N, Gobbi S, Corradi A et al. Consensus conference on laparoscopic appendectomy: development of guidelines. Colorectal Dis 2011; 3: 748–54.*
- 28 *Tai HC, Lin CD, Wu CC et al. Homemade transumbilical port: an alternative access for laparoendoscopic single-site surgery (LESS). Surg Endosc 2010; 24: 705–8.*
- 29 *Markides G, Subar D, Riyad K. Laparoscopic versus open appendectomy in adults with complicated appendicitis: a systematic review and meta-analysis. World J Surg 2010; 34: 2026–40.*
- 30 *Vettoretto N, Ismail A, Giovanetti M. A proposal for an evidence-based patients' selection in single incision laparoscopic appendectomy. J Minim Invasive Surg Sci 2012; 1: 164–5.*
- 31 *Alptekin H, Yilmaz H, Acar F et al. Incisional hernia rate may increase after single-port cholecystectomy. J Laparoendosc Adv Surg Tech A 2012; 22: 731–7.*