



Universiteit
Leiden
The Netherlands

Best practices in minimally invasive gynecology: making sense of the evidence

Sandberg, E.M.

Citation

Sandberg, E. M. (2018, April 25). *Best practices in minimally invasive gynecology: making sense of the evidence*. Retrieved from <https://hdl.handle.net/1887/61633>

Version: Not Applicable (or Unknown)

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/61633>

Note: To cite this publication please use the final published version (if applicable).

Cover Page



Universiteit Leiden



The following handle holds various files of this Leiden University dissertation:
<http://hdl.handle.net/1887/61633>

Author: Sandberg, E.M.

Title: Best practices in minimally invasive gynecology: making sense of the evidence

Issue Date: 2018-04-25

Chapter 4

Laparoendoscopic single-site surgery versus conventional laparoscopy for hysterectomy: a systematic review and meta-analysis

E.M. Sandberg, C.F. la Chapelle, M.M. van den Tweel,
J.W. Schoones, F.W. Jansen

Abstract

Purpose: To assess the safety and effectiveness of LESS compared to conventional hysterectomy.

Methods: The systematic review and meta-analysis was performed according to the MOOSE guideline, and quality of evidence was assessed using GRADE. Different databases were searched up to 4th of August 2016. Randomized controlled trials and cohort studies comparing LESS to the conventional laparoscopic hysterectomy were considered for inclusion.

Results: Of the 668 unique articles, 23 were found relevant. We investigated safety by analyzing the complication rate and found no significant differences between both groups [OR 0.94 (0.61, 1.44), $I^2=19\%$]. We assessed effectiveness by analyzing conversion risk, postoperative pain, and patient satisfaction. For conversion rates to laparotomy, no differences were identified [OR 1.60 (0.40, 6.38), $I^2=45\%$]. In 3.5% of the cases in the LESS group, an additional port was needed during LESS. For postoperative pain scores and patient satisfaction, some of the included studies reported favourable results for LESS, but the clinical relevance was non-significant. Concerning secondary outcomes, only a difference in operative time was found in favor of the conventional group [MD 11.3 min (5.45–17.17), $I^2=89\%$]. The quality of evidence for our primary outcomes was low or very low due to the study designs and lack of power for the specified outcomes. Therefore, caution is urged when interpreting the results.

Conclusion: The single-port technique for benign hysterectomy is feasible, safe, and equally effective compared to the conventional technique. No clinically relevant advantages were identified, and as no data on cost effectiveness are available, there are currently not enough valid arguments to broadly implement LESS for hysterectomy.

Introduction

Since the early 1990s, “minimally invasive surgery” (MIS) has been rapidly implemented into a variety of surgical disciplines. The main advantage of minimally invasive procedures is the absence of a large abdominal wound, which results in fewer wound-related complications, less postoperative pain, and a shorter hospital stay.¹ In an effort to extend these benefits, an increasing enthusiasm has emerged for the laparoendoscopic single-site surgery (LESS). In LESS, multiple laparoscopic instruments are placed through one single abdominal incision at the place of the umbilicus. The hypothesis is that single incision technique might offer advantages over the standard multi-port laparoscopy as abdominal wall trauma is decreased, potentially leading to less postoperative pain and improved cosmesis.²⁻⁴ The potential drawbacks of the single-port approach are a larger umbilical incision and the proximity of the instruments resulting in a technical challenge, especially for advanced surgery.^{5,6} It was only in 1991 that Pelosi et al. performed the first LESS hysterectomy,⁷ more than 20 years after the first publication on the LESS procedure in 1969.⁶ Reports have currently shown the feasibility of LESS surgery in many benign gynecologic procedures.^{8,9} However, it remains debatable whether this new technology has added value over the existing conventional laparoscopic technique and whether it should be broadly implemented for hysterectomy.

The proportion of laparoscopic hysterectomies (LH) has significantly increased the last decades: from 3% in 2002 to 36% in 2012 in the Netherlands,¹⁰ and similar numbers have been observed in other countries (United States¹¹ and Finland¹²). Regarding the proportion of hysterectomies performed using the LESS approach, no national overviews have been published on this topic so far. In some parts of the world, single-port hysterectomy seems well implemented. A retrospective single-hospital study from Korea showed for example that in 2013, 80% of their hysterectomies were LESS hysterectomies.¹³ Hysterectomy in general is one of the most performed advanced surgeries in gynecology with approximately 600,000 procedures a year in the United States.¹¹ As a result, defining the surgical approach with the most advantages is essential. In this light, the aim of this study is to provide a systematic review and meta-analysis of the current comparative studies evaluating specifically LESS hysterectomy and conventional laparoscopy. We particularly focused on the safety and effectiveness of the two techniques.

Materials and methods

Eligibility criteria, information source, search strategy

This systematic review was conducted according to the MOOSE guidelines.¹⁴ We identified original published studies through a search of Medline (PubMed version), EMBASE (Ovid version), Cochrane, Web of Science, Central, CINAHL, Academic Search Premier and Science Direct up to 4th of Augustus 2016 without restriction. The search terms included 'gynecology', 'hysterectomy', and all acronyms of LESS. The exact search terms are presented in supplemented material (Appendix 4.1). In addition, relevant studies cited in the reference lists of the selected papers were evaluated. Only comparative studies (randomized controlled trials, prospective and retrospective cohort studies) evaluating LESS versus hysterectomy for benign indications were considered for inclusion. LESS procedures had to be strictly performed through one single (umbilical) port as opposed to the conventional laparoscopic hysterectomy performed through more than one port. Studies on animals or patients aged <18 years were excluded as well as studies comprising endoscopic surgery with different techniques (e.g., hand- or robot-assisted, isobaric pneumoperitoneum). We also excluded descriptive review articles, surveys, technical reports, published abstracts without a full manuscript, reports from meetings, and trials with less than ten included participants per arm or 20 in total.

Study selection

Two reviewers independently screened the titles and abstracts for their relevance (ES and CC). Potentially relevant studies were obtained in full text and assessed for inclusion. We included studies wherein the effectiveness and/or safety of LESS compared to conventional laparoscopy for hysterectomy were investigated. To assess the safety of a procedure, we considered complication rates as primary outcome. Effectiveness refers to the potential success of a surgical procedure, and therefore, we considered: success rate (defined by the chance for a successful procedure without conversion to laparotomy and for the use of an additional port in the single-site group), postoperative pain scores, cosmetic outcomes, and patient satisfaction (including sexual function) as relevant primary outcomes. The following secondary perioperative outcomes were considered: operative time, intraoperative blood loss, and length of hospital stay. Although less important, these are also relevant identifiers for the effectiveness of a procedure.

Complications were defined according to the classification of the Dutch Society of Obstetrics and Gynecology and further divided into 'major complications' and 'minor complications'.¹⁵ Major complications included: major hemorrhage or hematoma (requiring transfusion);

urinary tract or bowel injury; pulmonary embolism; major anesthesia problems; vaginal cuff dehiscence; port site hernia; and re-operation. Minor complications were defined as hemorrhage (not requiring transfusion) or hematoma (with spontaneous drainage); infection to the chest, urinary tract, wound, pelvic, other, or pyrexia 38 °C; deep vein thrombosis; and other minor complication requiring treatment (including voiding dysfunction and ileus). We distinguished two types of conversion: an unintended conversion to laparotomy and the need for an additional port in the single-site group. The postoperative pain should be expressed on a self-reported scale¹⁶ (e.g., visual analog scale (VAS), numerical rating scale (NRS)), and for cosmetic outcomes, validated questionnaires should be used.

Data extraction

Outcome data as mentioned in the previous heading as well as study and patient characteristics were extracted from the included studies. These baseline findings included study design, number of included participants, country where the study was conducted, source of funding, relevant characteristics of the participants (age, body mass index, and uterine weight), description of the procedural setting, and experience of the physician. Data related to the defined outcomes were assessed for inclusion in the meta-analysis. Sensitivity analyses were performed for randomized studies and cohort studies when relevant subgroup analyses were accomplished for TLH and LAVH.

Assessment of risk of bias

The study limitations in randomized trials and observational studies were assessed using the checklists adapted from Guyatt et al.:¹⁷ (1) random sequence generation; (2) allocation concealment; (3) blinding of participants, surgeons, and investigators; (4) attrition bias: loss to follow-up (5) reporting bias: selective reporting and/or missing per protocol analysis; (6) other, e.g., use of non-validated outcome measures, difference in baseline characteristics between the groups and influence of co-interventions, or differing surgical experience in the compared procedures. For the first three points of the checklist, retrospective studies were rated as 'high risk', whereas attrition bias and reporting bias were marked as 'unclear', unless there was an additional reason to judge them as 'high risk'. The quality of evidence was then rated following the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach.¹⁸ The quality of evidence was classified into one of four categories: high quality, moderate quality, low quality, or very low quality. We used the online GRADE program (GRADEpro Guideline Development Tool [Software], McMaster University, 2015, developed by Evidence Prime, Inc., available from gradepro.org). Any discrepancies between reviewers were addressed by an open discussion.

Evidence synthesis and statistical analysis

Meta-analysis was conducted using Review Manager (Version 5.2. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012). For continuous data, we calculated mean differences (MDs) and standard deviations (SDs); for dichotomous data, we calculated odds ratio (OD) with their 95% confidence intervals (CIs). When summary data were missing, e.g., only the median and range were available, data were transformed as appropriate according to the definitions described by Hozo.¹⁹ We applied the random-effects model to combine data for meta-analysis.

Results

Study selection

Figure 4.1 shows the flow diagram of the literature selection for this review. The initial search yielded 668 unique references, and twenty-three studies fulfilled our inclusion criteria. Eleven studies compared LESS hysterectomy to conventional TLH,^{13;20-29} eleven studies compared LESS hysterectomy to LAVH,³⁰⁻⁴⁰ and in one study, both procedures were included.⁴¹ Two studies also included supra-cervical hysterectomies.^{20;21} The study by Koyanagi⁴² was excluded as all data were already included in another study by the same author.⁴⁰ The selected papers were published between 2010 and 2015.

Study characteristics

A total of 1,985 women in the LESS group and 2,466 women in the conventional hysterectomy were included in six randomized controlled trials,^{23;24;26;30;39;41} five prospective cohort studies,^{21;27;32;36;37} and 12 retrospective cohort studies.^{13;20;22;25;28;29;31;33-35;38,40} Twenty of the studies (86.9%) were performed in Asia (fifteen in Korea,^{13;23-25;27;28;31;32;34;35;37-39;41} one in China,²⁶ two in Japan,^{29;40} and two in Taiwan,^{30;33} and the other three studies originated from the United States,²⁰ Italy,²² and France.²¹ Fourteen studies had a single center design,^{20-24;26-30;33;36;37;39} one RCT was multi-center,⁴¹ and in the other eight studies, the setting was unclear.^{13;25;31;32;34;35;38,40} Fifteen studies stated that there was no potential conflict of interest to disclose,^{13;20-27;30-33;35;38} five studies reported financial support (from a grant of Samsung Medical Center,³⁹ from a grant of Korea Health Care technology,^{36;37} from Covidien,⁴¹ and from Kyung Hee University Research Fund³⁴), and three studies remained unclear about their potential conflicts.^{28;29;40}

Women in the LESS group aged between 40.3 and 53 years, their BMI ranged from 22.0 to 28.7 kg/m², and their uterine weight ranged from 105 to 642 grams. In the conventional

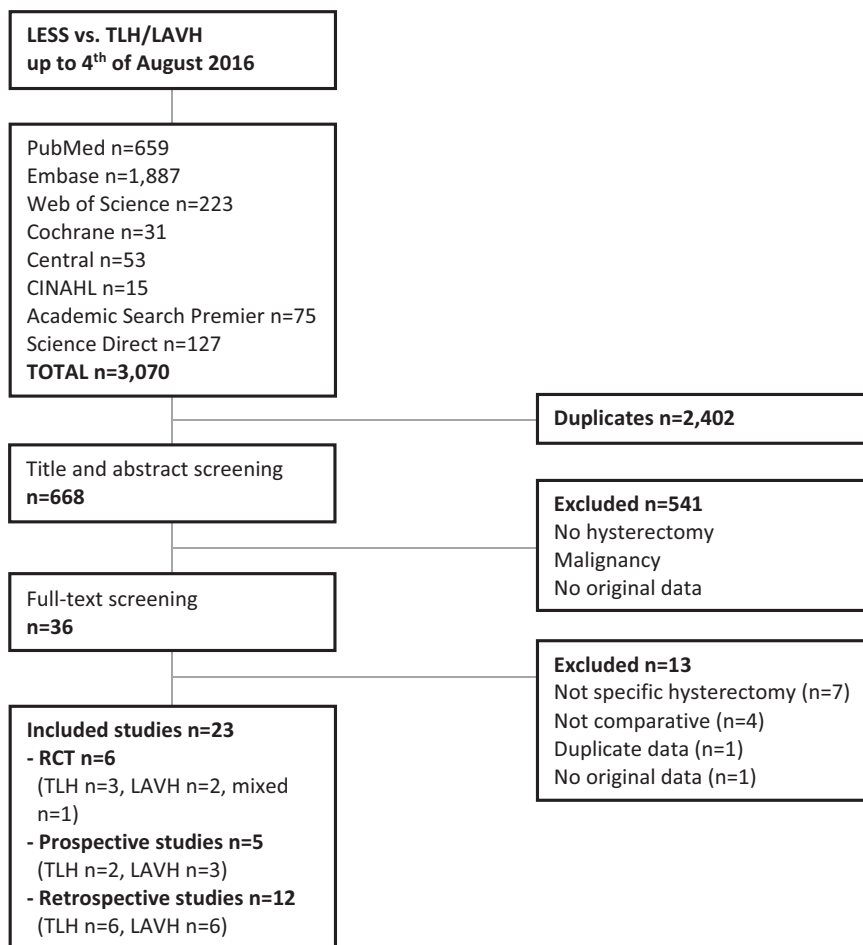


Figure 4.1: Flow diagram of the study selection.

group, the age range of the patients, their BMI, and uterine weight varied, respectively, between 41.26 and 63 years; 22.0–28.8 kg/m² and 9–613 g. In two studies from Lee et al., the same cohort was partially used: the smaller cohort study focused on outcomes of sexual function. We used the data from the largest cohort,³⁷ but for analysis of the outcome ‘sexual function’, we extracted the data from the partial cohort.³⁶

Risk of bias of the included studies

A summary of risk of bias for the individual studies is depicted in Figure 4.2. For the overview of GRADE findings, see Table 4.1.

| | Random sequence generation (selection bias) | Allocation concealment (selection bias) | Blinding of participants and personnel (performance bias) | Blinding of outcome assessment (detection bias) | Incomplete outcome data (attrition bias) | Selective reporting (reporting bias) | Other bias |
|---------------|---|---|---|---|--|--------------------------------------|------------|
| Angiono 2015 | + | + | + | + | ? | + | + |
| Chen 2011 | + | + | + | + | + | + | ? |
| Choi 2013 | + | + | + | + | ? | ? | + |
| Chung 2015 | + | + | + | + | + | + | + |
| Eom 2013 | + | + | + | + | + | + | ? |
| Fanfani 2012 | + | + | + | + | ? | ? | + |
| Fridman 2015 | + | + | + | + | ? | ? | + |
| Hong 2014 | + | + | + | + | ? | + | ? |
| Ichikawa 2011 | + | + | + | + | + | + | ? |
| Jung 2011 | + | + | + | + | ? | + | + |
| Jung 2011a | + | + | + | + | ? | ? | + |
| Kim 2010 | + | + | + | + | ? | ? | ? |
| Kim SM 2015 | + | + | + | + | ? | ? | ? |
| Kim TJ 2015 | + | + | + | + | + | + | + |
| Koyanagi 2011 | + | + | + | + | + | + | + |
| Lee 2011 | + | + | + | + | + | + | ? |
| Lee 2011a | + | + | ? | + | + | + | ? |
| Lee 2015 | + | + | + | + | ? | ? | + |
| Li 2012 | + | + | ? | ? | + | + | ? |
| Park 2015 | + | + | + | + | ? | ? | + |
| Song 2013 | + | + | + | + | + | + | + |
| Wang 2012 | + | + | + | + | ? | + | + |
| Yim 2010 | + | + | + | + | ? | ? | + |

Figure 4.2a: Risk of bias per study, LESS versus conventional laparoscopic hysterectomy.

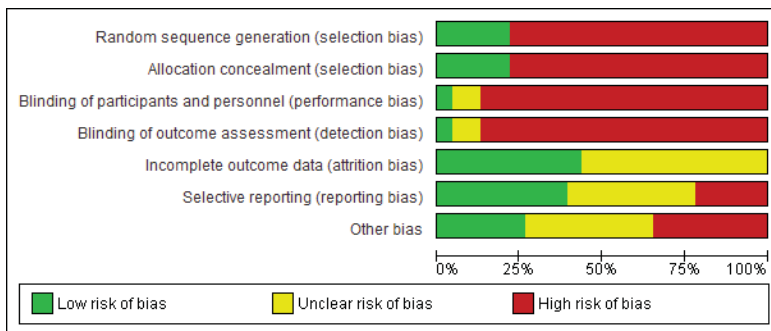


Figure 4.2b: Risk of bias summary LESS versus conventional laparoscopic hysterectomy.

Table 4.1: GRADE evidence LESS versus conventional laparoscopic hysterectomy

| | | LESS compared to conventional laparoscopic hysterectomy | | | | | | | | | | |
|---|----------------------|---|--------------|---------------------------|------------------|-----------------------------|-----------------------|-----------------|--------------------------|------------------------------|--|--|
| | | Quality assessment | | | | | Summary of findings | | | | | |
| No. of participants (studies) Follow-up | Risk of bias | Inconsistency | Indirectness | Imprecision | Publication bias | Overall quality of evidence | Study event rates (%) | | Relative effect (95% CI) | Anticipated absolute effects | | |
| | | | | | | | With conventional | With LESS | | Risk with conventional | Risk difference with LESS | |
| Complications major | | | | | | | | | | | | |
| 3,943 (23 observational studies) | serious ¹ | not serious | not serious | serious ² | none | ⊕○○○ VERY LOW | 121/2,153 (5.6%) | 94/1,790 (5.3%) | OR 0.94 (0.61 to 1.44) | 56 per 1,000 | 3 fewer per 1,000 (21 fewer to 23 more) | |
| Complications minor | | | | | | | | | | | | |
| 2,555 (13 observational studies) | serious ¹ | not serious | not serious | serious ² | none | ⊕○○○ VERY LOW | 61/1,368 (4.5%) | 40/1,187 (3.4%) | OR 0.76 (0.46 to 1.27) | 45 per 1,000 | 10 fewer per 1,000 (24 fewer to 11 more) | |
| Conversion to laparotomy | | | | | | | | | | | | |
| 4,124 (21 observational studies) | serious ¹ | not serious | not serious | very serious ² | none | ⊕○○○ VERY LOW | 8/2,289 (0.3%) | 22/1,835 (1.2%) | OR 1.60 (0.40 to 6.38) | 3 per 1,000 | 2 more per 1,000 (2 fewer to 18 more) | |

Table 4.1 continues on next page

Table 4.1: Continued

| LESS compared to conventional laparoscopic hysterectomy | | | | | | | | | | | |
|---|----------------------|----------------------|--------------|------------------------|---------------------|-----------------------------|-----------------------|-----------|------------------------------|---|--|
| Quality assessment | | | | | Summary of findings | | | | | | |
| No. of participants (studies) Follow-up | Risk of bias | Inconsistency | Indirectness | Imprecision | Publication bias | Overall quality of evidence | Study event rates (%) | | Anticipated absolute effects | | |
| | | | | | | | With conventional | With LESS | Relative effect (95% CI) | Risk with conventional | Risk difference with LESS |
| VAS score 24 h postoperatively | | | | | | | | | | | |
| 512 (5 RCTs) | serious ³ | serious ⁴ | not serious | not serious | none | ⊕⊕○○ LOW | 257 | 255 | - | The mean VAS score 24 hours postoperatively was -0.15 VAS | MD 0.14 VAS lower (0.58 lower to 0.28 higher) |
| Cosmetic outcomes | | | | | | | | | | | |
| 353 (3 RCTs) | serious ³ | not serious | not serious | serious ^{5,6} | none | ⊕⊕○○ LOW | 179 | 174 | - | The mean cosmetic outcomes was 0 | MD 0 (0 to 0) |
| Operative time | | | | | | | | | | | |
| 620 (5 RCTs) | not serious | not serious | not serious | serious ⁷ | none | ⊕⊕○○ MODERATE | 313 | 307 | - | The mean operative time was 119.6 min | MD 13.14 min more (1.69 more to 24.59 more) |

LESS compared to conventional laparoscopic hysterectomy

| Quality assessment | | Summary of findings | | | | | | | | | |
|--|--------------|---------------------|--------------|-------------|------------------|-----------------------------|-----------------------|-----------|--------------------------|---------------------------------------|--|
| No. of participants (studies) Follow-up | Risk of bias | Inconsistency | Indirectness | Imprecision | Publication bias | Overall quality of evidence | Study event rates (%) | | | Anticipated absolute effects | |
| | | | | | | | With conventional | With LESS | Relative effect (95% CI) | Risk with conventional | Risk difference with LESS |
| 620 (6 RCTs) | not serious | not serious | not serious | not serious | none | ⊕⊕⊕⊕ HIGH | 313 | 307 | - | The mean blood loss was 158 mL | MD 5.62 mL more (0.42 more to 10.82 more) |
| Length of stay | | | | | | | | | | | |
| 562 (4 RCTs) | not serious | not serious | not serious | not serious | none | ⊕⊕⊕⊕ HIGH | 284 | 278 | - | The mean length of stay was 3.81 days | MD 0.29 days fewer (0.74 fewer to 0.17 more) |

CI: Confidence interval; OR: Odds ratio; MD: Mean difference.

- ¹ Majority of studies are retrospective cohort studies.
- ² Wide confidence interval, crossing the line of no effect.
- ³ No blinding.
- ⁴ Differences between studies (in favor of conventional LH; in favor of LESS).
- ⁵ Different questionnaires.
- ⁶ Underpowered.
- ⁷ For TLH vs LESS a significant difference of 21 min was observed. For LAVH vs LESS a non significant difference of 2 min was observed.

Safety: complications

We found no differences between complication rates when comparing LESS hysterectomy to conventional hysterectomy when clustering into major complications (23 studies, OR 0.94 (0.61, 1.44), $I^2=19\%$, Figure 4.3a) and minor complications (13 studies, OR 0.76 (0.46–1.27), $I^2=11\%$, Figure 4.3b). Sub-analysis specific for TLH and LAVH showed no difference (data not shown). None of the studies reported a port site herniation, though only one study mentioned that they had collected data on herniation.²⁶

Effectiveness: success rate, postoperative pain scores, cosmetic results, and patient satisfaction

Conversion to laparotomy occurred in 22 of 1,835 patients (1.2%) in the LESS group, compared to 8 of 2,289 (0.35%) patients in the conventional group, which was not statistically significant (total 21 studies, OR 1.60 (0.40, 6.38), $I^2=45\%$, Figure 4.3c). The six RCTs included reported two conversions in both groups. For the 15 cohort studies, 17 of the 20 conversions in the LESS group were observed in one study.¹³ Reason for

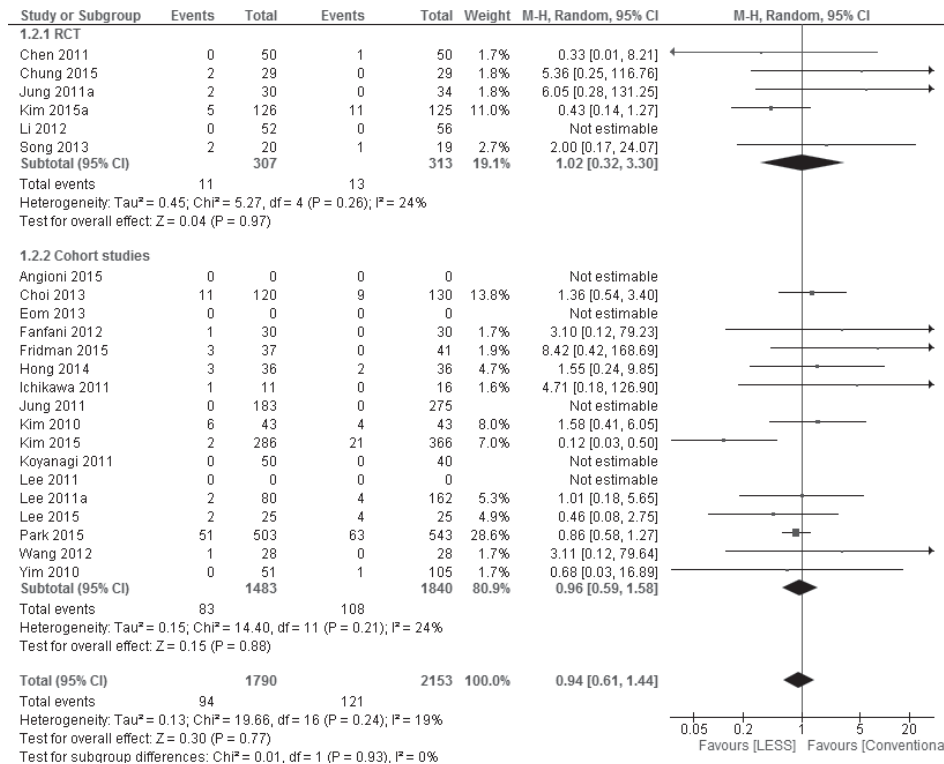


Figure 4.3a: Major complications, LESS versus conventional laparoscopic hysterectomy.

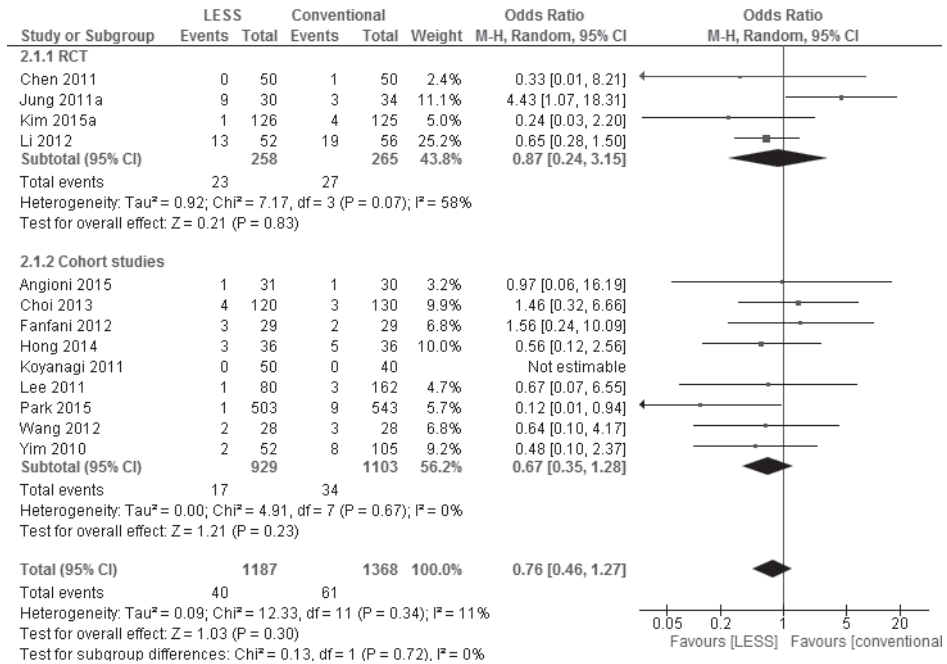


Figure 4.3b: Minor complications, LESS versus conventional laparoscopic hysterectomy.

conversions was extensive adhesions ($n=18$), bladder injury ($n=1$), bladder and bowel injury ($n=1$), retroperitoneal bleeding ($n=1$), and unspecified ($n=9$). When evaluating the rate of additional ports needed during LESS surgery, 48 of the 1,344 (3.5%) patients included had at least one additional port during LESS surgery versus one in the conventional group (0.06%).³⁸ Fourteen of these cases can be attributed to Fridman et al. where additional port was needed in 38% of the cases.²⁰ In the study by Jung et al. one patient had an additional port due to an incidental finding of an appendiceal mucinous adenoma.³⁴

Thirteen studies assessed the pain scores of their patients at various postoperative moments (direct after surgery up to one week) using VAS scores. Five of these studies were RCTs and one had appropriate double blinding. That specific RCT found no difference between the two groups at any of the reported moments (direct, 12, 24, and 48 h post-operative).²³ The pain scores direct, 12 and 24 h after surgery were most frequently studied and, therefore, pooled for meta-analysis. Data that analyzed pain scores in the recovery unit, thus immediately after surgery, showed significantly lower pain scores after LESS hysterectomy compared to conventional hysterectomy (5 studies, MD -1.09 (-1.66, -0.52), $I^2=80\%$, Figure 4.4a).^{21-23;28} The only randomized controlled trial included in this sub-analysis showed no difference between the two groups. At 12 h, a non-significant difference was

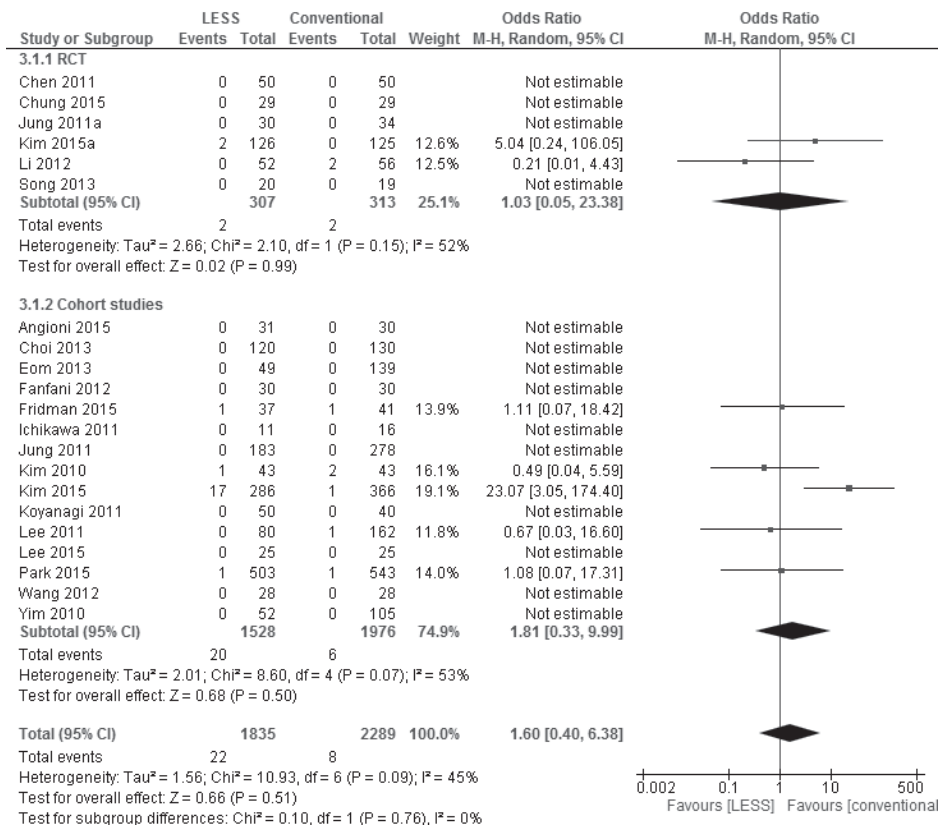


Figure 4.3c: Conversion to laparotomy, LESS versus conventional laparoscopic hysterectomy.

observed (5 studies, MD -0.19 (-0.41, 0.03), $I^2=0\%$, Figure 4.4b). At 24 h, meta-analysis showed a significant difference between the two groups (11 studies, MD -0.45 (-0.87, -0.03), $I^2=90\%$, Figure 4.4c).^{21;23;25;28} Though, the subgroup analysis including five RCTs showed non-significant results (MD -0.15 [-0.58, 0.28]. $I^2=64\%$). Ten studies reported on data regarding analgesic use.^{22-25;28;30;33;38;39;41} Chung et al. and Jung et al. showed that the LESS group requested significantly more (additional) analgesics, but the VAS scores revealed no difference.^{23;24} In contrast, the (rescue) analgesic requirement was significantly lower in the LESS group in four studies.^{22;28;30;38} Similarly, Hong et al. calculated a pain-relief score based on the amount and type of analgesic used and the effectiveness on pain relief and their results were also in favor of the single-port surgery.³³ Finally, Lee et al., Kim et al. and Song et al. showed no difference in analgesic use between the two groups.^{25;39;41}

Three studies reported on cosmetic results,^{21;39;41} and two used the validated Body Image Questionnaire at one, four and 24 week postoperative. Patients in the LESS group were

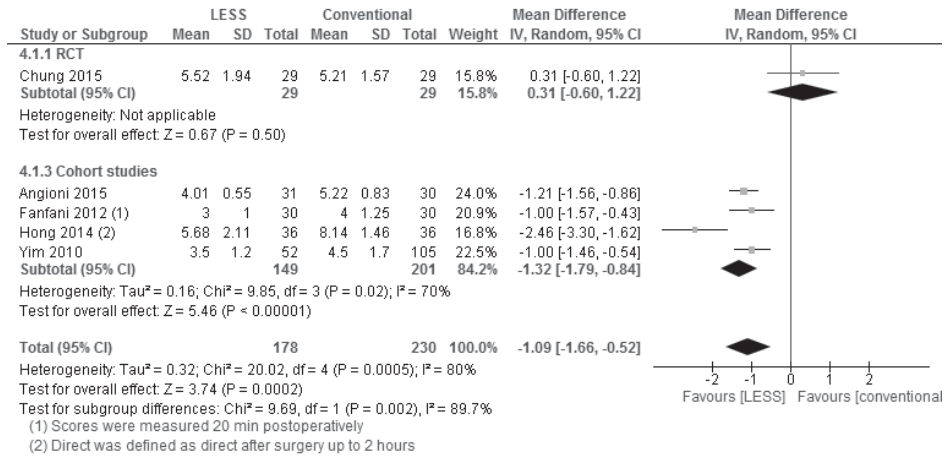


Figure 4.4a: Pain scores direct postoperative, LESS versus conventional laparoscopic hysterectomy.

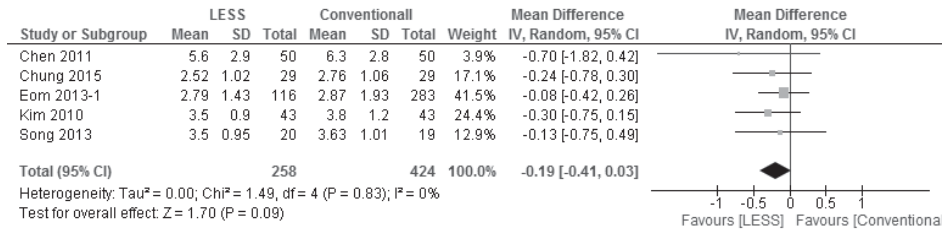


Figure 4.4b: Pain scores 12 hours postoperative, LESS versus conventional laparoscopic hysterectomy.

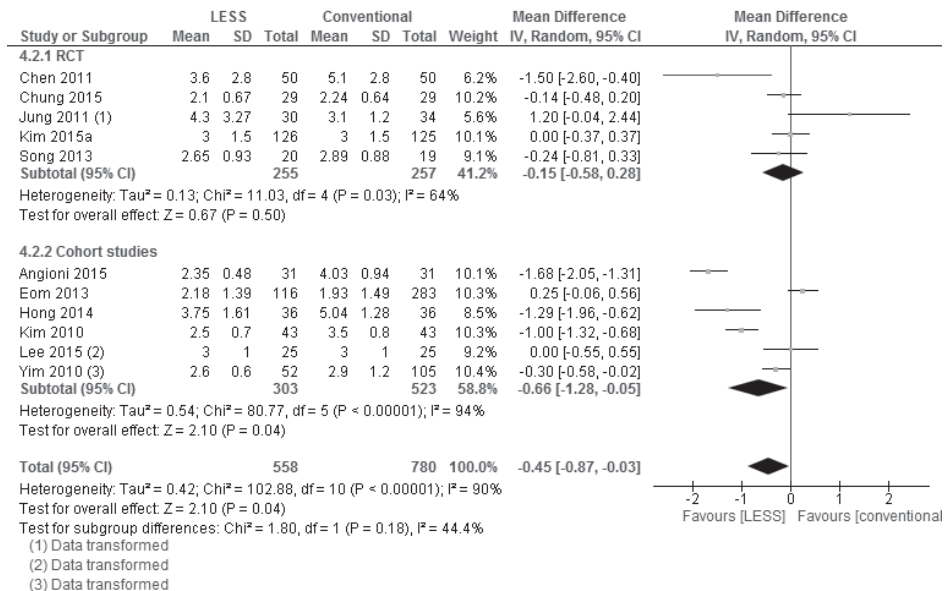


Figure 4.4c: Pain scores 24 hours postoperative, LESS versus conventional laparoscopic hysterectomy.

significantly more satisfied with their scars and had higher satisfaction with their own body at the three measured moments. Kim et al. studied the scar satisfaction using the patient and observer scar assessment scale (POSAS) one week and two months after surgery and showed no difference between the single-site group and the multi-port one. Li et al. studied patient satisfaction and demonstrated a higher patient satisfaction rate in the single-port group, although it was unclear which questionnaire was used.²⁶ Lee et al. compared the sexual function of premenopausal women by using the female sexual function index and showed no difference between women that underwent LESS compared to LAVH.³⁶

Secondary outcomes

The operative time was significantly longer in the single-port group compared to the multi-port group (20 studies, MD 11.3 min (5.45–17.17), $I^2=89%$, Figure 4.5a). When comparing separately TLH and LAVH, a significant difference of 21 minutes was seen in favor of the

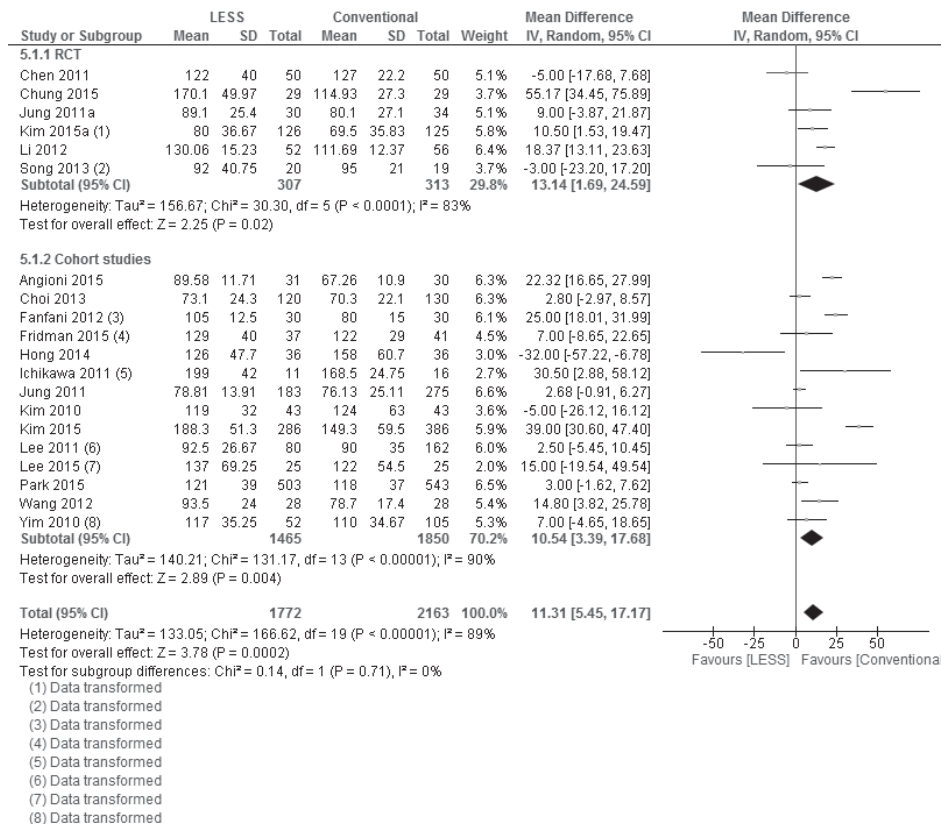


Figure 4.5a: Operative time, LESS versus conventional laparoscopic hysterectomy.

TLH group, compared to a non-significant difference of two minutes after LAVH (data not shown). No difference was seen for the intraoperative blood loss (19 studies, MD 1 mL (-6.03, -7.81), $I^2=27\%$, Figure 4.5b). For the length of hospital stay, a small significant difference was seen (15 studies, MD -0.22 (-0.43, -0.01), $I^2=86\%$, Figure 4.5c). This difference was not seen when looking separately at the RCTs and cohort studies.

Discussion

Main findings

In this systematic review, we evaluated the safety and effectiveness of LESS hysterectomy compared to the conventional laparoscopic hysterectomy (TLH and LAVH). Twenty-three studies on LESS versus conventional hysterectomy showed no differences for safety with very low quality evidence. Concerning effectiveness, very low quality evidence indicated no difference for the risk of conversion to laparotomy in the LESS group compared to

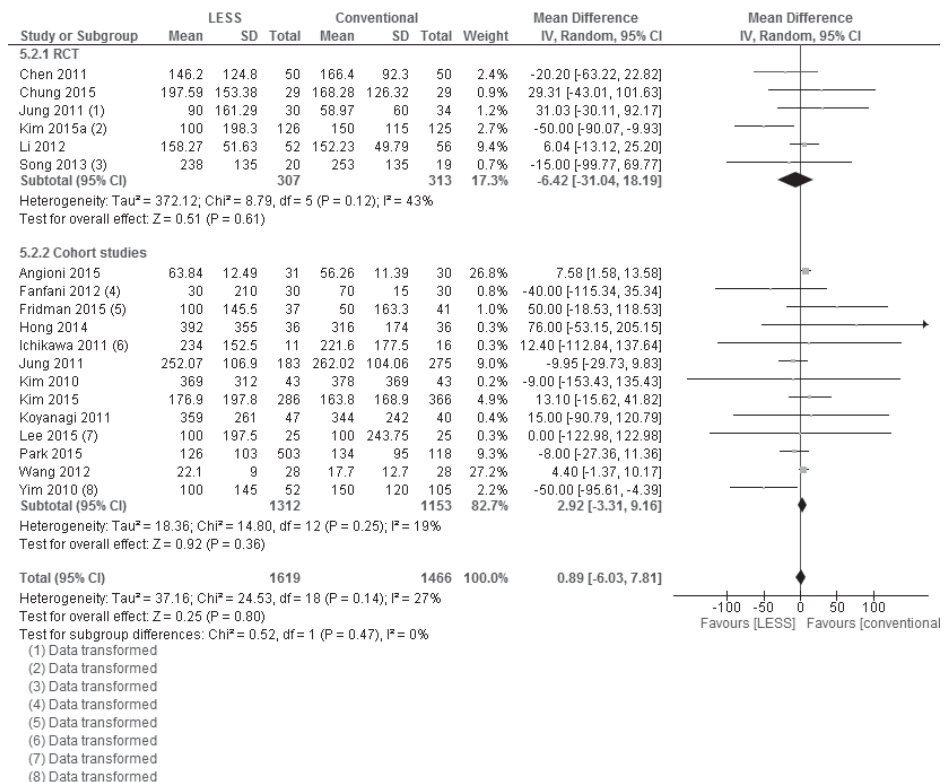


Figure 4.5b: Total blood loss, LESS versus conventional laparoscopic hysterectomy.

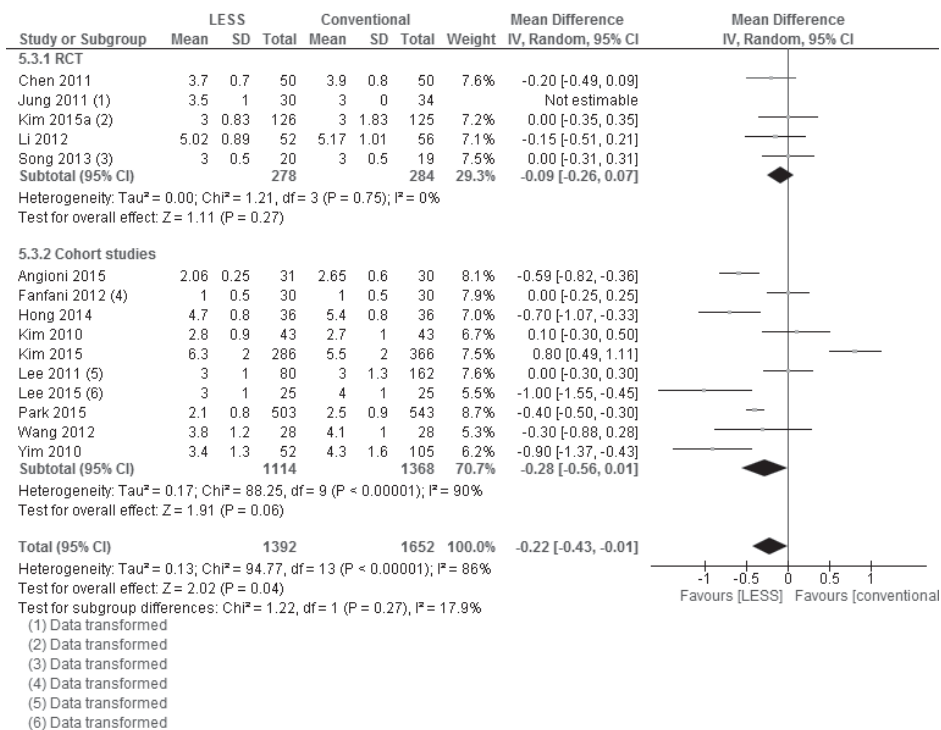


Figure 4.5c: Length of hospital stay, LESS versus conventional laparoscopic hysterectomy.

TLH and LAVH. In 3.5%, the LESS approach failed as an additional port was needed. For postoperative pain, low quality of evidence indicated a lower VAS score of 1.09 and 0.45, respectively, directly and 24 h after LESS hysterectomy, though with substantial statistical heterogeneity. Two out of three studies with low-quality evidence indicated a better cosmetic outcome after LESS versus conventional hysterectomy. A major shortcoming in these studies is the lack of a pre-operative assessment. Without a pre-operative assessment, it remains unclear whether there were any differences between the groups prior to their surgery. The third study, a RCT showed no difference with respect to scar satisfaction.

Strengths and limitations

Though there are some RCTs available comparing LESS to conventional hysterectomy, we decided to include other comparative study designs as well. The inclusion of non-RCT designs results in less homogenous groups, but when outcomes of interest are infrequent (e.g., conversion to laparotomy risk, complication risks); RCTs are rarely large and lengthy enough to measure infrequent outcomes accurately. Cohort studies facilitate a larger

study population and adequate power to identify significant differences. Therefore, the inclusion of study designs other than RCTs can be seen as a limitation but also as strength. In addition, to limit bias, we performed sensitivity analysis for the study design for the meta-analysis. Another strength of this review is the assessment of the quality of evidence using GRADE methodology. We believe that the use of GRADE results in additional clinical value of this review: GRADE optimizes the presentation of evidence for clinical practice. The results of this systematic review are strengthened through the findings of other reviews published on the subject that as well found no significant difference in the frequency of perioperative complications and postoperative pain scores.^{8,9,43} Though, other reviews described a higher rate of 'failures' in the LESS group. These studies defined 'failure' as the need to convert to laparotomy and/ or to add an extra port, without differentiating. We found that in 3.5% of the LESS procedures, an additional port was needed compared to <1% in the conventional procedures.

Interpretation

The feasibility of LESS surgery for benign gynecologic procedures seems proven.^{8,9} The meta-analyses in this review showed no significant differences in complication and conversion rate to laparotomy between LESS and conventional hysterectomy. Without substantial statistical heterogeneity, we consider these findings reliable. Besides complication risk, the pain experienced after surgery is an important consideration and usually an important argument in favor of LESS. Though, we did not find any clinically significant differences in postoperative pain. Directly and 24 h after LESS hysterectomy, a significant lower VAS score was observed. This difference was not observed when analyzing only the RCTs. Furthermore, the mean difference did not exceed 1.09 and studies have shown that a mean difference of 2 points on a 10-point scale should be considered as clinically relevant.⁴⁴ In addition, it cannot be excluded that enrolled patients in the study are biased with respect to their pain outcomes as, except in one study, the included patients were not blinded to the type of surgery. One single randomized controlled trial applied accurate blinding:²³ patients and anesthesiology staff who measured the postoperative pain scores did not know which type of approach had been performed and similar pain scores were found. Cosmetic outcomes are also suggested as important improvement in the single-site approach but surprisingly few studies on LESS hysterectomy reported on this topic.^{21,39,41} We judged the assessment in the two studies on patient satisfaction insufficient, since baseline assessment of body image and cosmetic satisfaction was not performed. The largest RCT published so far for hysterectomy reported no significant differences regarding scar satisfaction between the LESS and 'conventional' hysterectomy

group.⁴¹ When looking at studies published in other fields than benign gynecology, inconsistent results are found for the self-scar rating in patients who underwent LESS or conventional laparoscopic surgery.⁴⁵⁻⁴⁷ In Tuschy et al. patients who underwent conventional gynecological laparoscopy were asked which scar they would prefer to eliminate, and for most patients, it was the umbilical one.⁴⁸ In the study by Bush et al. patients were asked their aesthetic preference regarding scars, and no differences were observed between the single-site and conventional incisions.⁶ In LESS surgery, higher forces are applied on the umbilical port during tissue handling and irreversible umbilical deformation has been described.²⁹ It is also suggested that LESS would lead to a higher risk of port herniation as the opening of the umbilical port is larger.⁴⁹⁻⁵¹ Though, this could not be confirmed in the current literature, as within the short study follow-up, only one case of port herniation was reported.³¹

Evaluating the secondary surgical outcomes, a notable finding is the increased operative time found in the LESS versus conventional hysterectomy group: an overall mean difference of 11 minutes was observed, though with substantial heterogeneity. For the TLH, the mean difference was 21 minutes, whereas for the LAVH, a non-significant difference of two minutes was observed. The reason for the prolonged operative time during TLH is most probably related to the difference in surgical experience. For the LAVH, it makes sense that the operative time was similar as a large part of the LESS and conventional procedure is performed vaginally, thus using exactly similar techniques. It is well known that LESS surgery is technically more challenging^{8;9;43} and studies reporting on the learning curve in LESS have suggested that sufficient skills are acquired after 10 to 15³ up to 40 cases,⁵² especially when surgeons are already well-trained in laparoscopy. In five studies included in this review, the surgical experience of the surgeons was not described.^{13;28;30;35;38} In the other included studies, the experience of surgeons was defined by terms, such as 'very experienced', 'senior surgeon', or by the number of laparoscopic and/or LESS surgeries performed in one's career. Hence, it is difficult to interpret the impact of the skills on the outcomes. It is noteworthy mentioning that we found substantial differences in baseline characteristics between compared groups in the non-randomized studies (uterine weight,^{20;21;28} age,²⁰ BMI,³¹ previous surgeries, and co-morbidities^{28;38}). This could be explained by the surgeon's specific selection when performing a new technique in a non-randomized setting. Yet, an increased uterine weight, a high BMI, and/or previous surgical interventions are known to directly influence surgical outcomes⁵³ and this could lead to an overestimation of effectiveness, safety, and secondary outcomes (e.g., operative time, blood loss) for LESS outcomes. In addition, it should also be taken into account that 20 of the 23 studies originated from Asian, and therefore, the impact of Asian demographics should not be underestimated.

Remarkably, none of the included studies has taken the costs of the surgery into account, and currently, it is unknown if the LESS approach is cost effective. Despite the lack of data for LESS versus conventional hysterectomy, it can be reasoned that implementing the LESS technique in a hospital is costly as the conventional instruments do not fit and new instruments need to be purchased.

As seen with previous devices and or techniques,⁵⁴ implementing new technologies in the medical field is a challenge. In contrast to the introduction of new drugs, the latest techniques and devices are usually implemented in clinical practice without proper systematic evaluation regarding their safety, effectiveness, costs, and benefits. Advantages and disadvantages only become clear with the passage of time and after the implantation phase. Considering this, it is complex to answer the question whether the single-port surgery should be an additional possibility for the minimally invasive surgery. Most of studies in the review were single center and from the same region in the world, where a lot of experience has already been acquired with the LESS technique. Despite the amount of experience with LESS in these centers, there is still no clear added value.

In conclusion, current evidence shows that the single-port technique for benign hysterectomy (TLH and LAVH) is feasible, safe, and equally effective compared to the conventional technique. Caution is urged when interpreting the results of studies on LESS because the evidence is of *low to very low* quality. Potential benefits are sought in patient satisfaction, cosmetic satisfaction, and postoperative pain, but the small differences for these outcomes appear not to be of clinical relevance. Furthermore, surgeons and patients should be aware that in up to 3.5% of LESS hysterectomies an additional port is required resulting in failure of the “single-site” approach and affecting the less invasive purpose. As no clinically relevant advantages were identified, and no data on cost effectiveness were available, there are currently no solid arguments to implement the single-port technique worldwide.

References

- (1) Aarts JW, Nieboer TE, Johnson N, Tavender E, Garry R, Mol BW et al. Surgical approach to hysterectomy for benign gynaecological disease. *Cochrane Database Syst Rev* 2015;8:CD003677.
- (2) Fader AN, Cohen S, Escobar PF, Gunderson C. Laparoendoscopic single-site surgery in gynecology. *Curr Opin Obstet Gynecol* 2010;22(4):331-338.
- (3) Escobar PF, Starks D, Fader AN, Catenacci M, Falcone T. Laparoendoscopic single-site and natural orifice surgery in gynecology. *Fertil Steril* 2010;94(7):2497-2502.
- (4) Mencaglia L, Mereu L, Carri G, Arena I, Khalifa H, Tateo S et al. Single port entry - are there any advantages? *Best Pract Res Clin Obstet Gynaecol* 2013;27(3):441-455.
- (5) Fanfani F, Rossitto C, Gagliardi ML, Gallotta V, Gueli AS, Scambia G et al. Total laparoendoscopic single-site surgery (LESS) hysterectomy in low-risk early endometrial cancer: a pilot study. *Surg Endosc* 2012;26(1):41-46.
- (6) Bush AJ, Morris SN, Millham FH, Isaacson KB. Women's preferences for minimally invasive incisions. *J Minim Invasive Gynecol* 2011;18(5):640-643.
- (7) Pelosi MA, Pelosi MA, III. Laparoscopic hysterectomy with bilateral salpingo-oophorectomy using a single umbilical puncture. *N J Med* 1991;88(10):721-726.
- (8) Song T, Kim ML, Jung YW, Yoon BS, Joo WD, Seong SJ. Laparoendoscopic single-site versus conventional laparoscopic gynecologic surgery: a metaanalysis of randomized controlled trials. *Am J Obstet Gynecol* 2013;209(4):317-319.
- (9) Yang L, Gao J, Zeng L, Weng Z, Luo S. Systematic review and meta-analysis of single-port versus conventional laparoscopic hysterectomy. *Int J Gynaecol Obstet* 2016;133(1):9-16.
- (10) Driessen SR, Baden NL, van Zwet EW, Twijnstra AR, Jansen FW. Trends in the implementation of advanced minimally invasive gynecologic surgical procedures in the Netherlands. *J Minim Invasive Gynecol* 2015;22(4):642-647.
- (11) Wright JD, Herzog TJ, Tsui J, Ananth CV, Lewin SN, Lu YS et al. Nationwide trends in the performance of inpatient hysterectomy in the United States. *Obstet Gynecol* 2013;122(2 Pt 1):233-241.
- (12) Makinen J, Brummer T, Jalkanen J, Heikkinen AM, Fraser J, Tomas E et al. Ten years of progress--improved hysterectomy outcomes in Finland 1996-2006: a longitudinal observation study. *BMJ Open* 2013;3(10):e003169.
- (13) Kim SM, Park EK, Jeung IC, Kim CJ, Lee YS. Abdominal, multi-port and single-port total laparoscopic hysterectomy: eleven-year trends comparison of surgical outcomes complications of 936 cases. *Arch Gynecol Obstet* 2015;291(6):1313-1319.
- (14) Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. *Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA* 2000;283(15):2008-2012.
- (15) <http://www.nvog.nl/vakinformatie/Pati%C3%ABntveiligheid/Complicatieregistratie/default.aspx>
- (16) Joyce CR, Zutshi DW, Hrubes V, Mason RM. Comparison of fixed interval and visual analogue scales for rating chronic pain. *Eur J Clin Pharmacol* 1975;8(6):415-420.
- (17) Guyatt GH, Oxman AD, Vist G, Kunz R, Brozek J, Alonso-Coello P et al. GRADE guidelines: 4. Rating the quality of evidence--study limitations (risk of bias). *J Clin Epidemiol* 2011;64(4):407-415.
- (18) Guyatt GH, Oxman AD, Schunemann HJ, Tugwell P, Knottnerus A. GRADE guidelines: a new series of articles in the *Journal of Clinical Epidemiology*. *J Clin Epidemiol* 2011;64(4):380-382.
- (19) Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol* 2005;5:13.
- (20) Fridman D, Saraf S, Homel P, Wagner J. Single-incision laparoscopy as the primary approach to benign hysterectomies: A single-surgeon, single-year-experience with a retrospective control. *Journal of Gynecologic Surgery* 2015;31(2):78-82.
- (21) Angioni S, Pontis A, Pisanu A, Mereu L, Roman H. Single-port Access Subtotal Laparoscopic Hysterectomy: A Prospective Case-Control Study. *J Minim Invasive Gynecol* 2015;22(5):807-812.

- (22) Fanfani F, Fagotti A, Rossitto C, Gagliardi ML, Ercoli A, Gallotta V et al. Laparoscopic, minilaparoscopic and single-port hysterectomy: perioperative outcomes. *Surg Endosc* 2012;26(12):3592-3596.
- (23) Chung JH, Baek JM, Chung K, Park EK, Jeung IC, Chang HT et al. A comparison of postoperative pain after transumbilical single-port access and conventional three-port total laparoscopic hysterectomy: a randomized controlled trial. *Acta Obstet Gynecol Scand* 2015;94(12):1290-1296.
- (24) Jung YW, Lee M, Yim GW, Lee SH, Paek JH, Kwon HY et al. A randomized prospective study of single-port and four-port approaches for hysterectomy in terms of postoperative pain. *Surg Endosc* 2011; 25(8):2462-2469.
- (25) Lee J, Kim S, Nam EJ, Hwang SM, Kim YT, Kim SW. Single-port access versus conventional multi-port access total laparoscopic hysterectomy for very large uterus. *Obstet Gynecol Sci* 2015;58(3):239-245.
- (26) Li M, Han Y, Feng YC. Single-port laparoscopic hysterectomy versus conventional laparoscopic hysterectomy: a prospective randomized trial. *J Int Med Res* 2012;40(2):701-708.
- (27) Wang T, Chong GO, Park NY, Hong DG, Lee YS. Comparison study of single-port (Octoport) and four-port total laparoscopic hysterectomy. *Eur J Obstet Gynecol Reprod Biol* 2012;161(2):215-218.
- (28) Yim GW, Jung YW, Paek J, Lee SH, Kwon HY, Nam EJ et al. Transumbilical single-port access versus conventional total laparoscopic hysterectomy: surgical outcomes. *Am J Obstet Gynecol* 2010;203(1):26.
- (29) Ichikawa M, Akira S, Mine K, Ohuchi N, Iwasaki N, Kurose K et al. Evaluation of laparoendoscopic single-site gynecologic surgery with a multitrocar access system. *J Nippon Med Sch* 2011;78(4):235-240.
- (30) Chen YJ, Wang PH, Ocampo EJ, Twu NF, Yen MS, Chao KC. Single-port compared with conventional laparoscopic-assisted vaginal hysterectomy: a randomized controlled trial. *Obstet Gynecol* 2011; 117(4):906-912.
- (31) Choi YS, Park JN, Oh YS, Sin KS, Choi J, Eun DS. Single-port vs. conventional multi-port access laparoscopy-assisted vaginal hysterectomy: comparison of surgical outcomes and complications. *Eur J Obstet Gynecol Reprod Biol* 2013;169(2):366-369.
- (32) Eom JM, Choi JS, Choi WJ, Kim YH, Lee JH. Does single-port laparoscopic surgery reduce postoperative pain in women with benign gynecologic disease? *J Laparoendosc Adv Surg Tech A* 2013;23(12):999-1005.
- (33) Hong M-K, Wang J-H, Chu T-Y, Ding D-C. Laparoendoscopic single-site hysterectomy with Ligasure is better than conventional laparoscopic assisted vaginal hysterectomy. *Gynecology and Minimally Invasive Therapy* 2014;3(3):78-81.
- (34) Jung MH, Lee BY. Transumbilical single-port laparoscopic-assisted vaginal hysterectomy via 12-mm trocar incision site. *J Laparoendosc Adv Surg Tech A* 2011;21(7):599-602.
- (35) Kim TJ, Lee YY, Cha HH, Kim CJ, Choi CH, Lee JW et al. Single-port-access laparoscopic-assisted vaginal hysterectomy versus conventional laparoscopic-assisted vaginal hysterectomy: a comparison of perioperative outcomes. *Surg Endosc* 2010;24(9):2248-2252.
- (36) Lee JH, Choi JS, Hong JH, Joo KJ, Kim BY. Does conventional or single port laparoscopically assisted vaginal hysterectomy affect female sexual function? *Acta Obstet Gynecol Scand* 2011;90(12):1410-1415.
- (37) Lee JH, Choi JS, Jeon SW, Son CE, Hong JH, Bae JW. A prospective comparison of single-port laparoscopically assisted vaginal hysterectomy using transumbilical GelPort access and multiport laparoscopically assisted vaginal hysterectomy. *Eur J Obstet Gynecol Reprod Biol* 2011;158(2):294-297.
- (38) Park JY, Nho J, Cho IJ, Park Y, Kim DY, Suh DS et al. Laparoendoscopic single-site versus conventional laparoscopic-assisted vaginal hysterectomy for benign or pre-invasive uterine disease. *Surg Endosc* 2015;29(4):890-897.
- (39) Song T, Cho J, Kim TJ, Kim IR, Hahm TS, Kim BG et al. Cosmetic outcomes of laparoendoscopic single-site hysterectomy compared with multi-port surgery: randomized controlled trial. *J Minim Invasive Gynecol* 2013;20(4):460-467.

- (40) Koyanagi T, Motomura S. Single-incision laparoscopically assisted vaginal hysterectomy: Operative outcomes and its learning curve. *Exp Ther Med* 2011;2(5):867-871.
- (41) Kim TJ, Shin SJ, Kim TH, Cho CH, Kwon SH, Sung S et al. Multi-institution, Prospective, Randomized Trial to Compare the Success Rates of Single-port Versus Multiport Laparoscopic Hysterectomy for the Treatment of Uterine Myoma or Adenomyosis. *J Minim Invasive Gynecol* 2015;22(5):785-791.
- (42) Koyanagi T, Motomura S. Transumbilical single-incision laparoscopic surgery: application to laparoscopically assisted vaginal hysterectomy. *Arch Gynecol Obstet* 2011;283(2):305-309.
- (43) Pontis A, Sedda F, Mereu L, Podda M, Melis GB, Pisanu A et al. Review and meta-analysis of prospective randomized controlled trials (RCTs) comparing laparo-endoscopic single site and multiport laparoscopy in gynecologic operative procedures. *Arch Gynecol Obstet* 2016;29(4):567-577.
- (44) Giraudeau B, Rozenberg S, Valat JP. Assessment of the clinically relevant change in pain for patients with sciatica. *Ann Rheum Dis* 2004;63(9):1180-1181.
- (45) Song T, Park JY, Kim TJ, Lee YY, Choi CH, Lee JW et al. A prospective comparative study of cosmetic satisfaction for three different surgical approaches. *Eur J Obstet Gynecol Reprod Biol* 2015;190:48-51.
- (46) Park SK, Olweny EO, Best SL, Tracy CR, Mir SA, Cadeddu JA. Patient-reported body image and cosmesis outcomes following kidney surgery: comparison of laparoendoscopic single-site, laparoscopic, and open surgery. *Eur Urol* 2011;60(5):1097-1104.
- (47) Eom JM, Ko JH, Choi JS, Hong JH, Lee JH. A comparative cross-sectional study on cosmetic outcomes after single port or conventional laparoscopic surgery. *Eur J Obstet Gynecol Reprod Biol* 2013;167(1): 104-109.
- (48) Tuschy B, Berlit S, Brade J, Sutterlin M, Hornemann A. Gynaecological laparoscopic surgery for benign conditions: do women care about incisions? *Eur J Obstet Gynecol Reprod Biol* 2013;169(1):84-87.
- (49) Kadar N, Reich H, Liu CY, Manko GF, Gimpelson R. Incisional hernias after major laparoscopic gynecologic procedures. *Am J Obstet Gynecol* 1993;168(5):1493-1495.
- (50) Gunderson CC, Knight J, Ybanez-Morano J, Ritter C, Escobar PF, Ibeanu O et al. The risk of umbilical hernia and other complications with laparoendoscopic single-site surgery. *J Minim Invasive Gynecol* 2012;19(1):40-45.
- (51) Mayol J, Garcia-Aguilar J, Ortiz-Oshiro E, De-Diego Carmona JA, Fernandez-Represa JA. Risks of the minimal access approach for laparoscopic surgery: multivariate analysis of morbidity related to umbilical trocar insertion. *World J Surg* 1997;21(5):529-533.
- (52) Paek J, Kim SW, Lee SH, Lee M, Yim GW, Nam EJ et al. Learning curve and surgical outcome for single-port access total laparoscopic hysterectomy in 100 consecutive cases. *Gynecol Obstet Invest* 2011;72(4):227-233.
- (53) Driessen SR, Sandberg EM, la Chapelle CF, Twijnstra AR, Rhemrev JP, Jansen FW. Case-Mix Variables and Predictors for Outcomes of Laparoscopic Hysterectomy: A Systematic Review. *J Minim Invasive Gynecol* 2016;23(3):317-330.
- (54) Laparoscopic Uterine Power Morcellation in Hysterectomy and Myomectomy: FDA Safety Communication <http://www.fda.gov/medicaldevices/safety/alertsandnotices/ucm393576.htm>

Appendix 4.1: Literature search LESS versus conventional hysterectomy Search up to 4th of August 2016

PubMed:

("gynaecology"[All Fields] OR "gynecology"[MeSH Terms] OR "gynecology"[All Fields] OR gynaecologic[All Fields] OR gynecologic[All Fields] OR "Genital Diseases, Female"[Mesh] OR "female genital disease"[all fields] OR "female genital diseases"[all fields] OR "Gynecologic Surgical Procedures"[Mesh]) AND (("Single Incision Laparoscopic Surgery"[All Fields] OR "laparo-endoscopic single-site surgery"[all fields] OR "One port umbilical surgery"[all fields] OR "Natural orifice transluminal endoscopic surgery"[all fields] OR "Single-incision minimally invasive surgery"[all fields] OR "Single laparoscopic incision transabdominal surgery"[all fields] OR "Single-port access"[all fields] OR "Single-port laparoscopy"[all fields] OR "Single-port incisionless conventional equipment-utilizing surgery"[all fields] OR "Umbilical laparoendoscopic single-site surgery"[all fields]) OR ("laparoscopy"[MeSH Terms] OR "laparoscopy"[All Fields] OR "laparoscopic"[All Fields] OR laparoendoscopic[All Fields]) AND (("single"[All Fields] AND (site[All Fields] OR port[all fields] OR incision[all fields] OR umbilical[all fields] OR transumbilical[all fields])) OR (single-port[all fields] OR single-site[all fields] OR single-incision[all fields])) AND ("surgery"[Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms])) AND ("2012/05/01"[PDAT] : "3000/12/31"[PDAT])

Embase:

(gynaecolog*.mp. OR gynecolog*.mp. OR exp gynecology/ OR exp gynecologic disease/ OR female genital disease*.mp. OR exp gynecologic surgery/) AND (("Single Incision Laparoscopic Surgery".mp. OR "laparo-endoscopic single-site surgery".mp. OR "One port umbilical surgery".mp. OR "Natural orifice transluminal endoscopic surgery".mp. OR "Single-incision minimally invasive surgery".mp. OR "Single laparoscopic incision transabdominal surgery".mp. OR "Single-port access".mp. OR "Single-port laparoscopy".mp. OR "Single-port incisionless conventional equipment-utilizing surgery".mp. OR "Umbilical laparoendoscopic single-site surgery".mp.) OR ((exp laparoscopy/ OR exp laparoscopic surgery/ OR "laparoscopy".mp. OR "laparoscopic".mp. OR laparoendoscopic.mp.) AND (("single".mp. AND (site.mp. OR port.mp. OR incision.mp. OR umbilical.mp. OR transumbilical.mp.)) OR (single-port.mp. OR single-site.mp. OR single-incision.mp.)) AND (exp surgical technique/ OR surgery.mp. OR surgical.mp.)) AND (201236 OR 201237 OR 201238 OR 201239 OR 20124* OR 20125* OR 2013* OR 2014* OR 2015* OR 2016*).ew

