Reviews

Total Versus Subtotal Hysterectomy: Systematic Review and Meta-analysis of Intraoperative Outcomes and Postoperative Short-term Events

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ABSTRACT

Purpose: The benefits and disadvantages of cervical extraction during hysterectomy are unclear in the literature. We intended to compare total (TH) with subtotal or supracervical (SH) hysterectomy regarding intraoperative and postoperative outcomes (quality of life, sexual function, pain and cyclical bleeding).

Methods: A systematic literature search for randomized controlled trials was conducted on MEDLINE, LILACS, Cochrane CENTRAL, SCOPUS, EMBASE, Clinicaltrials.gov databases, and conference abstracts (AAGL, AUGS, ICS) from 1970 to November 2017. Two reviewers independently searched, selected and then combined the articles. Meta-analyses were conducted using a random-effect model. The risk of bias was evaluated using the Cochrane's Collaboration tool.

Findings: Eleven studies were included involving 1523 patients. The analyses showed that the events operative time (mean difference: 12.88 minutes, 95%CI [7.45, 18.30] $p < 0.000001$), hospital stay (MD .44 days, 95%CI [0.11, 0.77] $p = 0.0008$), and intraoperative blood loss (MD 81.06 ml, 95%CI [9.16, 152.97] $p = 0.03$) favored SH over TH, although the rate of blood transfusion did not differ between the groups. Conversely, TH group had less cyclical vaginal bleeding over SH (1.2% versus 14.1%; RR .14 95%CI [0.05, 0.43] $p = 0.0006$) during one-year follow up. Persistent pain and sexual satisfaction rates, and quality of life scores were similar in both total and subtotal hysterectomy groups up to 12 months follow up.

Implications: Overall perioperative outcomes favored the preservation of the cervix during hysterectomy but women that had SH are more susceptible to present cyclical vaginal bleeding mimicking menstruation. Those factors should be taken into account along with patient's needs and expectations prior to selecting the procedure. (*Clin Ther*. 2019;41:768–789)

Keywords: total, subtotal, supracervical, hysterectomy, short-term events, sexual function, quality of life, meta-analysis, review.

INTRODUCTION

Hysterectomy is the most common surgical procedure in non-pregnant women in the USA with about 433,621 operations being performed annually.[1] Removing or not the cervix during hysterectomy is still a matter of debate. Some trials reported that women undergoing total hysterectomy (TH) had less cyclical bleeding.[2] On the other hand, new cohort studies suggested that subtotal hysterectomy (SH) is associated to lower re-operation rate,[3] better sexual function and quality of life than TH.[4,5] However, a cross-sectional survey with 115 US women concluded that cervical removal did not impact sexual function

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according to the patients' view.[6] A multicenter retrospective chart analysis comparing laparoscopic-assisted vaginal total hysterectomy with laparoscopic subtotal hysterectomy for nonprolapsed uterus found no difference in perioperative outcomes.[7]

Systematic reviews have been performed to address this topic. The review by Gimbel et. al. in 2007[8] that included RCTs and observational studies found that SH had less estimated blood loss and overall intra and postoperative complications over TH. The Cochrane Collaboration leaded by Lethaby et al (2009) published the first systematic review and meta-analysis of only RCTs (three trials involving 733 patients) which compared SH and TH outcomes according to time frames.[9] It was shown that SH had a shorter operative time, lower estimated blood loss, and lower febrile morbidity rate than TH group. An update in 2012[10] found that postoperative urinary retention was less frequent while cyclical vaginal bleeding was higher in SH group compared to TH up to two-year follow up.

In order to help patients and physicians during the decision-making process, evidence-based medicine is imperative. More than five years have elapsed since the last update on the outcomes post hysterectomy with or without removing the cervix. Therefore we decided to conduct this systematic review with meta-analysis addressing intra and postoperative outcomes and short-term events (up to 12 months of follow-up) including pain, vaginal bleeding, sexual function and quality of life in women that underwent SH or TH for benign conditions.

MATERIALS AND METHODS

Search strategy and study selection

Our systematic review is registered at PROSPERO as CRD42016049502 and it is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines.[11] Two reviewers (GFA and MCMF) independently performed the search in the following databases (PubMed/Medline, Lilacs, Cochrane Central Register for Clinical Trials, SCOPUS, EMBASE, clinicaltrials.gov), and conference abstracts (2010–2017 – American Association for Gynecological Laparoscopists – AAGL; International Continence Society – ICS; American Urogynecologic Society - AUGS) from 1970 to November 2017. We also reviewed all references from previous published meta-analyses.[8,10] Language was not considered a barrier to retrieve the results. The search strategy (available at Supplementary Material) followed the PICOS questions, used combined relevant terms and MeSH (Medical Subject Headings of the National Library of Medicine) descriptors and the criteria as follow:

1 Population: women that underwent hysterectomy for benign conditions such as leyomyioma, endometriosis, adenomyosis, benign tumors and cysts, pelvic pain;
2 Intervention: total abdominal, laparoscopic or vaginal hysterectomy;
3 Comparator: subtotal abdominal or laparoscopic hysterectomy;
4 Outcomes: operative time, intraoperative estimated blood loss, blood loss requiring transfusion, urinary tract injury, febrile morbidity, hospital stay, hospital readmission, return to normal activity, pelvic pain, cyclical vaginal bleeding, dyspareunia, sexual satisfaction, quality of life;
5 Study design: randomized controlled trial;
6 Timing: outcomes considered up to 12 months postoperative.

Data extraction

Two reviewers (GFA and MCMF) independently selected and then combined the articles. Both investigators extracted the data using a previously tested extraction spreadsheet. Any discrepancy was resolved by consensus between the reviewers or after discussion with a third author (RAC). Initially, the reviewers evaluated the title and abstract of all studies that were found using the search strategy. Full texts were evaluated if the reports did not provide sufficient information in the title and abstract. A list of potential studies for inclusion in the systematic review was generated. The references in the reviews and the excluded articles were examined to identify studies that possibly could not be captured using the primary search strategy. Quality of evidence was assessed by the GRADE rsummary of findings which summarizes the level of evidence and the relative or absolute impact of each analysed intervention.[12]

Extracted data included details on study title, authors, year of publication, study design, inclusion and exclusion criteria, randomization, patients' characteristics, surgical procedure, outcome measurements and their results.

Outcome definitions

We analyzed intraoperative and postoperative short-term events. We evaluated outcomes up to one-year follow-up considering that longer follow-up would increase the potential influence of other cofounding variables such as ageing and other eventual medical conditions in the results other than consequence of the surgical procedure per se. Primary outcomes were: operative time (minutes), intraoperative blood loss (ml), blood transfusion rate, urinary tract injury rate, postoperative febrile morbidity rate (anal or axillary temperature equal or above 37.8 degrees Celsius in the first 48 hours after surgery), hospital stay (days), readmission related to the surgery (absolute numbers) and time to return to normal activity (weeks). Secondary outcomes were postoperative persistent pelvic pain, cyclical vaginal bleeding considered as irregular or occasional or even small bleeding reported by the patient mimicking normal menstruation, dyspareunia and sexual satisfaction rates using validated and/or non validated questionnaires, and general quality of life by Short Form SF-36 scale (scores ranging from 0-100),[13] and/or Psychological General Well Being (PGWB) questionnaires (scores ranging from 0-100)[14] both in which higher score means better outcome.

Data synthesis and statistical analysis

A random-effects meta-analysis model was applied to compensate that the surgical studies compared different techniques carried out by several groups of surgeons. Assuming a common effect size was difficult. Inverse-variance weighting was used to pool estimates from selected studies. RevMan 5.3 was used (Cochrane Collaboration) to combine the results across the studies. Heterogeneity was evaluated using Q test (χ^2 chi square test) which assesses whether observed differences in results are compatible with chance alone. A low P value (or a large chi-squared statistic relative to its degree of freedom) provides evidence of heterogeneity of intervention effects (variation in effect estimates beyond chance) and I^2 statistic,[15,16] Thresholds for the interpretation of I^2 can be misleading since the importance of inconsistency depends on several factors. According to the Cochrane handbook,[12] a rough guide to interpretation is as follows: 0% to 40%: might not be important, 30% to 60%, may represent moderate heterogeneity, 50% to 90%, may represent substantial heterogeneity, 75% to 100%: considerable heterogeneity. The importance of the observed value of I^2 depends on magnitude and direction of effects and strength of evidence for heterogeneity.. Statistical significance was defined at the 0.05 level.

Dichotomous data were expressed as risk ratios (RR) with 95% confidence intervals (CI). For continuous data we used standard deviation (SD) that was either available in the text or calculated using data from the text, expressed as mean difference (MD) between groups with 95% CI. Subgroup analysis was done according to the surgical procedure (e.g., open abdominal vs. vaginal vs. laparoscopy) when possible, considering that differences may occur according to the surgical approach.

All articles were evaluated using the Cochrane's Collaboration tool in order to assess the risk of bias within the clinical trials.[12]

RESULTS

Characteristics of the studies included

A total of 3,991 articles were retrieved after searching all databases and conference abstracts.[17] Figure 1 presents the search strategy conducted by the reviewers. After removing duplicates (784 publications), 3, 207 articles were screened and 12 studies were selected[2,18–27] for meta-analysis with a total of 1,523 patients (1,275 women underwent abdominal hysterectomy, and 248 laparoscopic hysterectomy); complimentary data from some of the selected primary studies were taken from other four publications.[28–31] Table 1 displays the characteristics of the included studies.

Quality assessment and risk of bias

Figures 2a and b summarize the risk of bias and its sources on the included studies. One study was double-blinded,[25] the others were either non blinded[21] or with no blindness method information.[18,23,26,27] Selection bias was a major concern and we extensively tried to reduce it by searching for information on the method of randomization. Randomization process was not reported in three studies,[18,27,32] while other four used block randomization.[20,22,24,33] *Berner et. al.*[2] reported large variability on the results of women with endometriosis and adenomyosis. All studies relied on documentation of events instead of direct

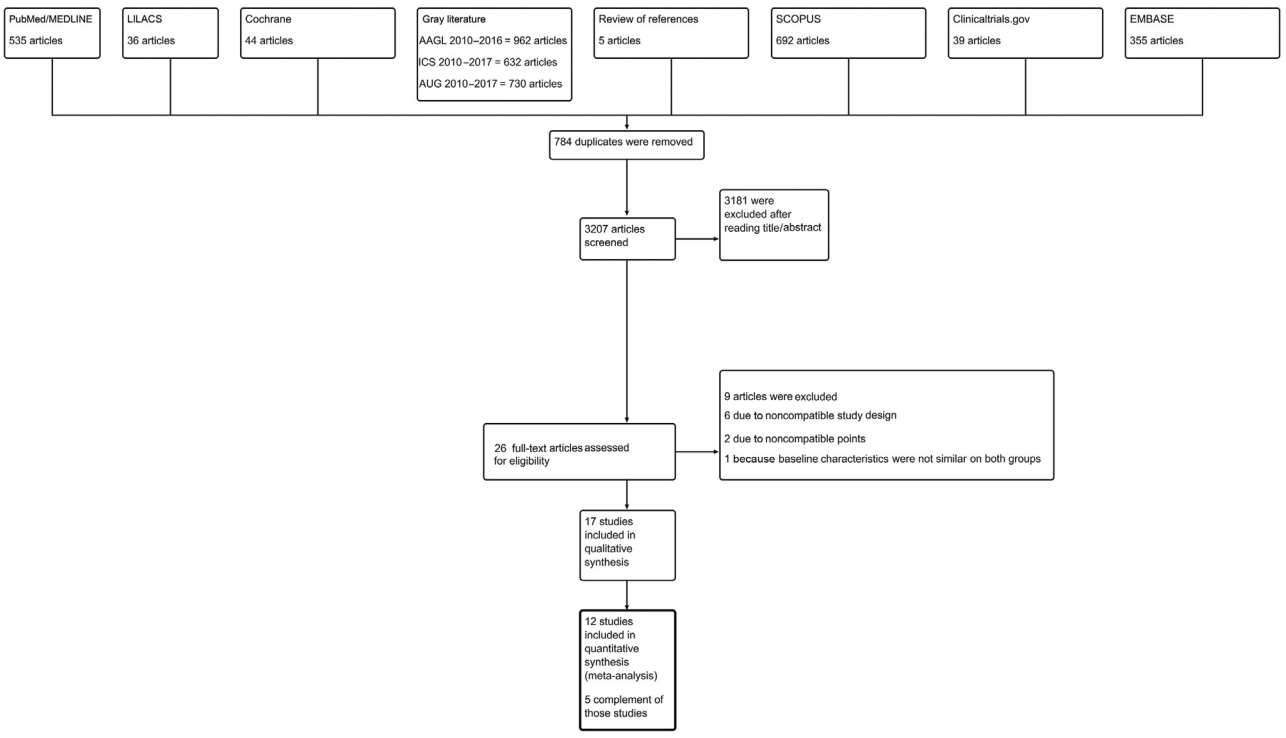

Figure 1. Flow chart of the study selection.

measurement by investigators, what may lead to some variability.

One important point on the analysis of studies is the lack of external validity that may exist by either a small number of included surgeons,[34] or a very homogeneous population. The TOSH group studies[22,28] tried to reduce the lack of external validation selecting women from different ethnicities, geographic locations and surgeons. *Thakar et.al.*[25] included two centers, *Gorlero et. al.*[21] conducted a study where all procedures were conducted by the same surgeon, and *Asnafi et al.*[18] included only two surgeons operating the subjects. Eight trials were unicentric.[2,19,20,22–24,26,27]

GRADE summary of findings showed that all outcomes had high risk of bias mainly because most studies were not double blinded and some were not clear about allocation concealment. Low quality of evidence were detected for febrile morbidity, blood loss during surgery, operative time, return to normal activities, dyspareunia and hospital stay events mainly due to the high heterogeneity among the studies (>39%). Blood loss requiring transfusion, urinary tract infection, readmission rate, persistent pelvic pain, cyclic vaginal bleeding, satisfaction with sex, health and mental scores and quality of life data were considered of moderate quality of evidence (Table 2). This table also allowed a better analysis of the results and if they were clinically relevant, especially in continuous outcomes.

There might be concerns that the analysis of the combined results from both laparoscopic and abdominal hysterectomy is not appropriate due to differences between the techniques. However, we presented the findings of both approaches in single forest plots containing either the overall combined data or data from the subgroup analyses. Those would allow the readers to have a better overview of each approach separately or together. Also what we could observe is that despite the differences between

Table 1. List and description of the studies included in the metaanalysis

Study	Inclusion and exclusion	Participants	Intervention	n	Participants characteristics	Outcomes
Asnafi 2010[2]	Inclusion: age >35; premenopausal, symptomatic uterine fibroids Exclusion: age >50, pregnant, malignancy, >100kg, diabetes mellitus, VH, geographically not accessible	Randomization method: not reported Centers: 1 Design: parallel group blinding: Not reported but unlikely Randomized: n:150 Analyzed: n: 150 Power calculation: yes Intention to treat: yes	Total abdominal Subtotal abdominal	100 50	Age 45.6 (6.5) Preoperative hemoglobin 11.9 (0.13) Age 43.3 (7.0) Preoperative hemoglobin 11.9 (0.19)	Fever, anemia, duration of hospitalization, changes in sexual function
Asgari 2009[26]	Inclusion: Age range 35–60, weight <100kg, normal pap smear Exclusion: obesity, malignancies, diabetes mellitus, pulmonary dysfunction, contraindication for laparoscopy, chronic pelvic pain or severe endometriosis, single and widower patients, connective tissue disease or with clear POP	Randomization method: not specified Centers: 1 Design: parallel group Blinding: no Randomized: n: 45 Analyzed: n: 45 Power calculation: no Intention to treat : not specified	Total laparoscopic Subtotal laparoscopic	25 20	Age 45.6 (5.58) Weight 69.36 (6.73) Age 44.45 (4.50) Weight 66.73 (8.79)	Perioperative events and sexual function analysis
Berner 2015[2]	Inclusion criteria: cyclical pelvic pain Exclusion criteria: do not speak Norwegian, CIN, malignancy, substantial enlarged uterus, POP, menopausal women, requiring extraction of both ovaries, severe endometriosis	Randomization method : permuted blocks Centers:1 Design: parallel group Blinding: single Randomized: n: 62 Analyzed: n: 32 Intention to treat: yes	Total laparoscopic Subtotal laparoscopic	31 31	Age 45.1 (5.6) BMI 26 (6.1) Quality of life (SF-36) 64 (17.4) Age 44.5 (4.2) BMI 26.3 (5.1) Quality of life (SF-36) 66.3 (21.6)	Primary: reduction of cyclic pelvic pain Secondary: patient satisfaction and quality of life (SF-36 questionnaire)

Table 1. (*Continued*)

Study	Inclusion and exclusion	Participants	Intervention	n	Participants characteristics	Outcomes
Learman, 2003[22] Kupperman, 2005[28]	Inclusion: premenopausal with symptomatic fibroids or with abnormal bleed and minimum 3 mo. trial of hormonal therapy, age > 45, FSH < 30 mIU/ml and negative biopsy within 6 mo. for endometrial hyperplasia or cancer Exclusion: age > 50, pregnant, decide to future pregnancy, genital cancer, dysplasia, endometrial hyperplasia, VH, not accessible for 4 years	Randomizations method : Random numbers generated by computer in blocks Centers:4 Design: parallel group Blinding: single Randomized: n: 135 Analyzed: n: 135 Intention to treat: yes Dropout rate: reached 10% SAH and 4% TAH in follow up	Total abdominal Subtotal abdominal	67 68	Age 41.8 (5.2) Weight 83.5 (19.8) >100kg 19% Pelvic pain 21% Age 41.8 (5.1) Weight 82.8 (24.3) >100kg 26% Pelvic pain 29%	Urinary, pelvic, sexual and quality of life symptoms (SF-36 questionnaire) Readmission rate Gastrointestinal Cardiac Pulmonary Wound complication Neurologic problem Other Total admission
Ellstrom, 2010[19]	Inclusion: premenopausal women scheduled for AH for benign disorders Exclusion: previous cervical dysplasia; planned oophorectomy, POP	Randomization: allocation from sealed opaque envelopes Centers: 1 Design: parallel group Blinding: no Randomized: n: 132 Analyzed: n: 102 Intention to treat: yes	Total abdominal Subtotal abdominal	52 50	Age 44.8 (4.2) BMI 26.2 (4.5) Married 84.6% No steady sexual partner 13.5% Age 44.9 (4.3) BMI 25.5 (4.8) Married 78% No steady sexual partner 14%	Changes in sexual health and changes in psychological wellbeing (PGWB questionnaire)
Morelli, 2007[23]	Inclusion: premenopausal with symptomatic fibroids or with abnormal bleed and minimum 3 mo. trial of hormonal therapy, age > 45, FSH < 30 mIU/ml and negative biopsy within 6 mo. for	Randomization: Computer generated numerical sequence Centers:1 Design: parallel group Blinding: single	Total laparoscopic	70 71	Age 41.8 (5.1) Weight 83.5 (19.8) >100kg 18% Pain or pelvic pressure 20%	Surgical characteristics, readmission in 24 mo, metrorrhagia, pelvic pain, pelvic

(*continued on next page*)

Table 1. (*Continued*)

Study	Inclusion and exclusion	Participants	Intervention	n	Participants characteristics	Outcomes
	endometrial hyperplasia or cancer Exclusion: age > 50, pregnant, decide to future pregnancy, genital cancer, dysplasia, endometrial hyperplasia, VH, not accessible for 4 years	Randomized: n: 141 Analyzed: n: 141 Intention to treat: no, but yes for surgical events	Subtotal laparoscopic		Age 41.8 (5.1) Weight 82.8 (24.3) >100kg 25% Pain or pelvic pressure 28%	or vesical pressure, lumbar pain, urge incontinence, stress incontinence, incomplete bladder emptying
Gimbel 2003[20] Zobbe 2004[31]	Inclusion: women scheduled for AH for benign disease Exclusion: LH, VH, dysplasia, POP, malignancy, diabetes, participation in other research projects, unable to read/write Danish, urological operation, cervix problems, neuropsychiatric problems, chronic alcoholism	Randomization method: restricted, computer generated block Centers: 11 Design: parallel group Blinding: no Randomized: n: 319 Analyzed: n: 277 Power calculation: yes Intention to treat: yes	Total abdominal Subtotal abdominal	140 136	Age 47.6 (15.1) BMI > 25 42% Pelvic pain 3% Age 46.6 (6.4) BMI > 25 47% Pelvic pain 5%	Primary: perceived urinary incontinence Secondary: quality of life (SF36), constipation, POP, satisfaction with sexual life, pelvic pain, vaginal bleeding, postoperative complications, dyspareunia
Ghanbari 2007[27]	Inclusion: sexually active women, no malignancy no other genetic disease Exclusion criteria: presence of malignant lesions, neurological disease, abnormal pap smear, chronic pelvic pain, dyspareunia, incapacitated diseases like cancer	Randomization method: not reported Centers: 1 Design: parallel group Randomized: n: 50 Analyzed: n: 50 Power calculation: no Intention to treat: no	Total abdominal Subtotal abdominal	25 25	Age 45.7 (5.8) BMI 26.4 (3.7) Abnormal bleeding 92% Age 46.6 (4.9) BMI 26.4 (3.7)	Surgical complications and postoperative sexual function

Table 1. (*Continued*)

Study	Inclusion and exclusion	Participants	Intervention	n	Participants characteristics	Outcomes
Gorlero 2008[21]	Inclusion: Women requiring an AH for a benign indication Exclusion: 2nd or 3rd degree uterine prolapse, age >75, malignancy, BMI > 29, previous pelvic surgery, endometriosis, chronic pelvic pain, abnormal cervical smear, psychiatric disorders	Randomization method: computer generated numbers Centers: 1 Design: parallel group Randomized: n: 117 Analyzed: n:105 Power calculation: no Intention to treat: no	Total abdominal Subtotal abdominal	54 51	Age 49 (6) BMI 24.1 (3) Age 46 (4) BMI 25 (2.3)	Primary: women's satisfaction (questionnaire on sexual activity, body image and health status) Secondary: surgical complications, postoperative recovery
Persson 2010[24] Persson 2010[29]	Inclusion: AH for benign condition, Swedish speaker, preservation of at least one ovary Exclusion: malignancy, rapidly growing fibroids where malignancy could not be ruled out, GnRH analogues, postmenopausal women without HRT, severe psychiatric disorders	Randomization method: random numbers table with block randomization according to center Centers: 8 Design: parallel group Randomized: n: 200 Analyzed: n: 178 Intention to treat: yes	Total abdominal Subtotal abdominal	84 94	Age 45.7 (5.1) BMI 25.8 (14.3) Age 45.9 (5) BMI 25.7 (3.6)	Primary: general psychological wellbeing (PGWB questionnaire) Secondary: postoperative complications (including stress incontinence), surgical and clinical outcomes during surgery
Thakar 2002[25] Thakar 2004[30]	Inclusion: AH for benign indication Exclusion: age > 60, suspected carcinoma, weight >100 kg, previous pelvic surgery, known endometriosis, abnormal cervical smears, symptomatic POP, symptomatic urinary incontinence	Randomization method: computer generated numbers and sealed opaque envelopes opened after surgical incision Centers: 2 Design: parallel group Blinding: double	Total abdominal Subtotal abdominal	146 133	Age 44 (6) Weight 72 (15) Age 43 (6) Weight 70 (15)	Primary: bowel, bladder and sexual function Secondary: postoperative complications; intraoperative outcomes and complications,

(*continued on next page*)

Table 1. (*Continued*)

Study	Inclusion and exclusion	Participants	Intervention	n	Participants characteristics	Outcomes
		Randomized: n: 279 Analyzed: n: 279 Power calculation: yes Intention to treat: yes				readmission rate, changes in psychological outcomes and health status/ quality of life (SF-36 questionnaire)

AH = abdominal hysterectomy; BMI = body mass index; CIN = cervical intraepithelial neoplasia; FSH = follicle-stimulating hormone; GnRH = gonadotropin-releasing hormone; HRT = hormone replacement therapy; LH = laparoscopic hysterectomy; PGWB = Psychological General Well-Being; POP = pelvic organ prolapse; SF-36 = Short Form SF-36; VH = vaginal hysterectomy.

both approaches the proportion of the differences was the same on either laparoscopic or abdominal approach and the heterogeneity between subgroups groups were 0%, with the exception of return to normal activities event (71% heterogeneity).

Primary outcomes

Operative time

Eight studies in a total of 991 women evaluated the operative time which favored SH even though the mean difference was only 13 minutes shorter than TH (MD 12.88 min, 95%CI [7.45, 18.30] p < 0.00001, i^2 = 74%)[2,21–27] (Figure 3a). The very similar operative time described by *Morelli et al*[23] (mean difference of only 5 minutes between laparoscopic TH and SH) may have influenced the overall finding. Operative time event favored the cervix preservation regardless of the surgical approach: open abdominal or laparoscopic and the heterogeneity between subgroups was i^2 = 0% (Figure 3a).

Estimated blood loss and blood transfusion

Overall intraoperative blood loss event favored SH over TH (MD 81.06 ml, 95%CI [9.16, 152.97] p = 0.03, i^2 = 65%, 5 studies, 780 women).[22,23,25,27] Abdominal approach accounted for those results (p = .02) specially due to *Ghanbari et al*[27] that reported a 300 ml higher blood loss in TH compared to SH. Blood loss did not differ either maintaining or removing the cervix via laparoscopy (Figure 3b).

On the other hand, estimated blood loss difference did not reflect into numbers of patients that needed blood transfusion which were similar in both SH and TH groups regardless of the surgical approach (RR 0.77 95%CI [0.43 1.39] p = 0.62, i^2=0% 6 studies, 850 women)[21–26] (Figure 3c) and the heterogeneity between subgroups i^2=0%.

Reported urinary tract injury

Four studies evaluated this event.[20,22,23,27] Urinary tract injury was reported in 6 out of 300 (2%) TH patients and 2 out of 299 (0.2%) SH patients. There was no statistical difference between TH and SH techniques regarding this event (RR 3.33 95%CI [0.68, 16.34] p=0.14, i^2=0%) even if the analysis was conducted separately according to the type of surgical approach (i^2=0% between subgroups) (Figure 3d).

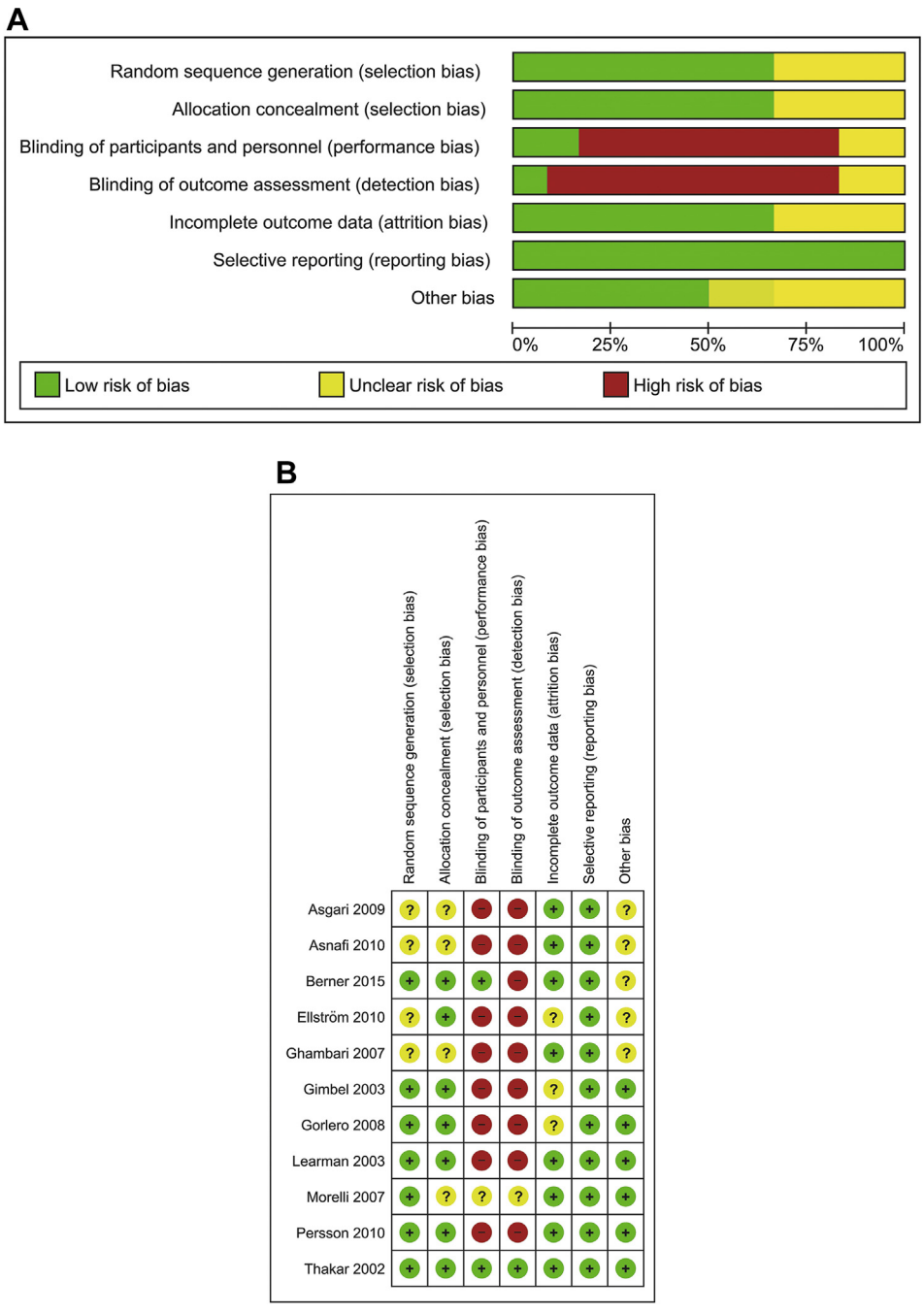

Figure 2. a: Risk of bias graph: percentage of each risk of bias item across all included studies. b: Risk of bias summary: study judgment about each risk of bias item.

Table 2. Grade summary of findings

Outcomes	Anticipated Absolute Effects* (95% CI)		Relative Effect (95% CI)	No. of Participants (Studies)	Certainty of the Evidence (GRADE)	Comments
	Risk With Subtotal Hysterectomy	Risk With Total Hysterectomy				
	The mean in minutes was 85.7	The mean in minutes in the intervention group was 12.88 higher (7.45 higher to 18.3 higher)	—	991 (8 RCTs)	⨁⨁◯◯ LOW	High risk of bias High heterogeneity
Intraoperative blood loss	The mean measured in milliliters was 406.4	The mean measured in milliliters in the intervention group was 81.06 higher (9.16 higher to 152.97 higher)	—	780 (5 RCTs)	⨁⨁◯◯ LOW	High risk of bias High heterogeneity
Blood loss requiring transfusion	57 per 1.000	44 per 1.000 (25 to 80)	RR, 0.77 (0.43 to 1.39)	880 (6 RCTs)	⨁⨁⨁◯ MODERATE	High risk of bias
Urinary tract injury	3 per 1.000	11 per 1.000 (2 to 55)	RR, 3.33 (0.68 to 16.34)	599 (4 RCTs)	⨁⨁⨁◯ MODERATE	High risk of bias
Febrile morbidity	92 per 1.000	136 per 1.000 (81 to 229)	RR, 1.48 (0.88 to 2.49)	1133 (7 RCTs)	⨁⨁◯◯ LOW	High risk of bias High heterogeneity
Hospital stay	The mean hospital stay was 3.5 d	The mean hospital stay in the intervention group was 0.44 higher (0.11 higher to 0.77 higher)	—	1080 (8 RCTs)	⨁⨁◯◯ LOW	High risk of bias High heterogeneity
Readmission	93 per 1.000	73 per 1.000 (43 to 123)	RR, 0.78 (0.46 to 1.32)	831 (4 RCTs)	⨁⨁⨁◯ MODERATE	High risk of bias
Return to normal activities	The mean return to normal activities was 12.47 d	The mean return to normal activities in the intervention group was 0.56 higher (0.42 lower to 1.53 higher)	—	355 (3 RCTs)	⨁⨁◯◯ LOW	High risk of bias High heterogeneity
Persistence of pelvic pain	136 per 1.000	139 per 1.000 (103 to 185)	RR, 1.02 (0.76 to 1.36)	1041 (6 RCTs)	⨁⨁⨁◯ MODERATE	High risk of bias
Cyclical vaginal bleeding	142 per 1.000	20 per 1.000 (7 to 61)	RR, 0.14 (0.05 to 0.43)	955 (6 RCTs)	⨁⨁⨁◯ MODERATE	High risk of bias

Table 2. (*Continued*)

Outcomes	Anticipated Absolute Effects* (95% CI)		Relative Effect (95% CI)	No. of Participants (Studies)	Certainty of the Evidence (GRADE)	Comments
	Risk With Subtotal Hysterectomy	Risk With Total Hysterectomy				
Dyspareunia	83 per 1.000	98 per 1.000 (32 to 308)	RR, 1.18 (0.38 to 3.70)	452 (2 RCTs)	⊕⊕◯◯ LOW	High risk of bias High heterogeneity
Satisfaction with sex	708 per 1.000	679 per 1.000 (587 to 792)	RR, 0.96 (0.83 to 1.12)	504 (3 RCTs)	⊕⊕⊕◯ MODERATE	High risk of bias
Physical score	The mean physical score was 42.64	The mean physical score in the intervention group was 0.46 higher (1.28 lower to 2.2 higher)	—	652 (3 RCTs)	⊕⊕⊕◯ MODERATE	High risk of bias
Mental score	The mean mental score was 29.03	The mean mental score in the intervention group was 0.59 higher (0.85 lower to 2.02 higher)	—	831 (4 RCTs)	⊕⊕⊕◯ MODERATE	High risk of bias
Quality of life	The mean quality of life was 47.25	The mean quality of life in the intervention group was 0.34 lower (0.96 lower to 0.28 higher)	—	540 (4 RCTs)	⊕⊕⊕◯ MODERATE	High risk of bias

MD = mean difference; RCT = randomized controlled trial; RR = risk ratio.
Patient or population: Benign conditions. A Meta-analysis.
Intervention: Total hysterectomy.
Comparison: Subtotal hysterectomy.
*The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).
GRADE Working Group grades of evidence: High certainty—We are very confident that the true effect lies close to that of the estimate of the effect. Moderate certainty—We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Low certainty—Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect. Very low certainty—We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

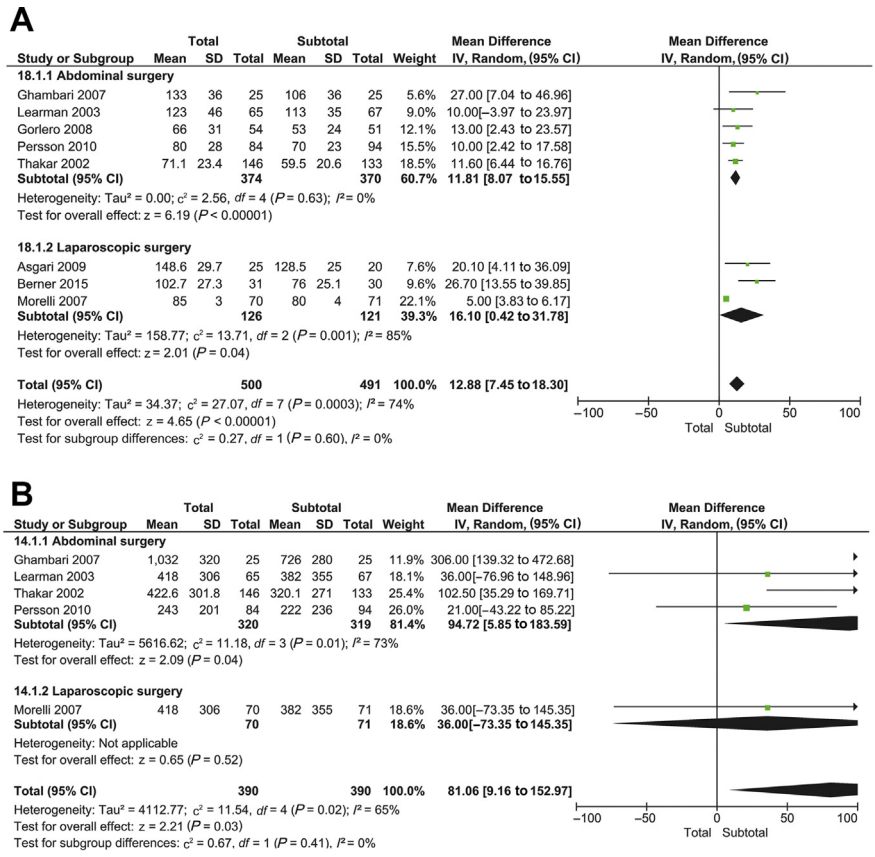

Figure 3. a: Forest plots comparing operative time between TH and SH. b: Forest plots comparing estimated blood loss between TH and SH. c: Forest plots comparing blood loss requiring transfusion between TH and SH. d: Forest plots comparing urinary tract injury between TH and SH.

Febrile morbidity

There was no statistical difference between TH and SH techniques regarding number of patients who had fever (14.5% versus 9.1% respectively; RR 1.48 95% CI [0.88, 2.49] p=0.14, i^2=50%, 7 studies, 1133 women)[18,20–23,25], 35 (Figure 4a). Among the included studies, Thakar et al[25] independently found higher rate of febrile morbidity in TH (19%) over SH (6%) groups (28/146 versus 8/133, respectively). The heterogeneity between subgroups was 0%.

Hospital stay

Overall statistical difference favoring SH was observed for length of hospital stay (MD 0.44 days; 95%CI [0.11, 0.77] p = 0.008, i^2=69%, 8 studies, 1080 women)[18,21–27] (Figure 4b). When the surgical approaches were evaluated separately, only open abdominal approach corroborated for shorter hospital stay in SH over TH groups (AH p =.04) but not through laparoscopy (LH p = .12) (Figure 4b). The heterogeneity between subgroups was 0%.

Readmission related to surgery

Number of patients readmitted due to complications related to surgery was similar either for TH or SH (7.3% versus 9.3%; RR 0.78, i^2=16%, 95%CI [0.46, 1.32] p = 0.49, 4 studies; 831 women)[20,22,23,25] regardless of surgical approach (subgroup heterogeneity i^2 = 0%) (Figure 4c).

Return to normal activities

Overall TH and SH groups were similar regards to time to return to regular activities (as sick leave or time out of work) (MD 2.29 days, 95%CI [-1.83,

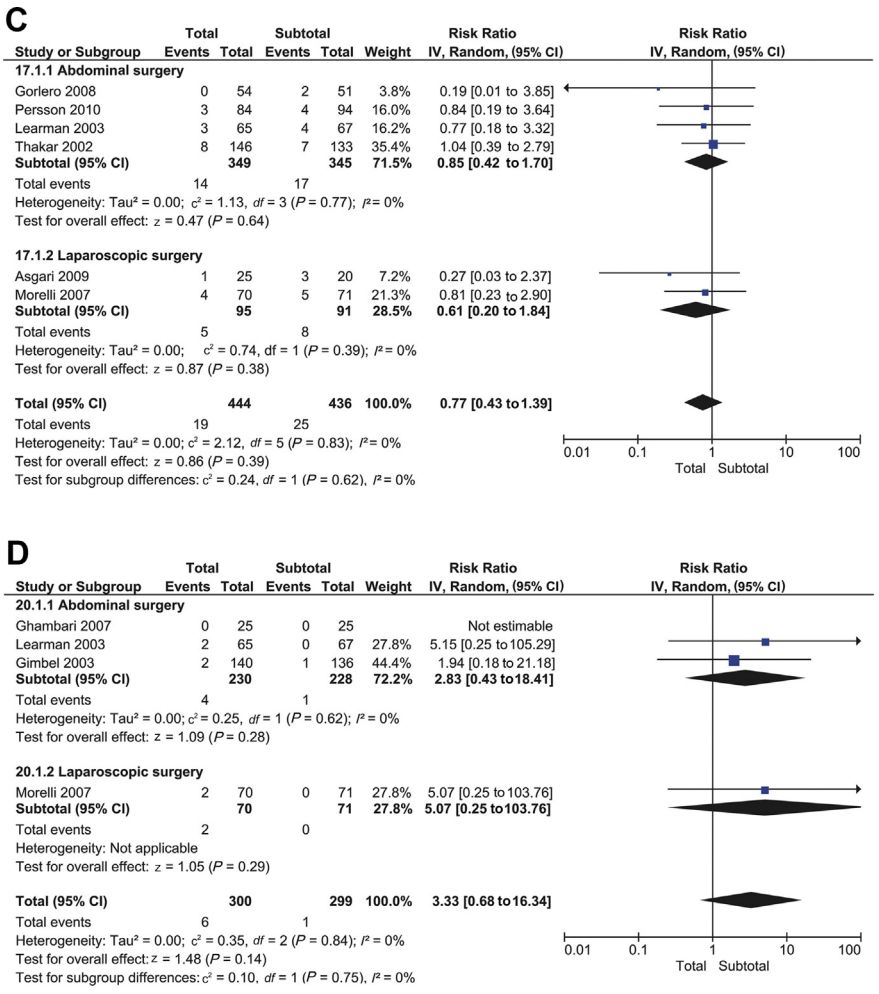

Figure 3. (*continued*).

6.41] p = 0.28, i^2=45%, 3 studies, 355 women)[22,24,26] (Figure 4d). Difference was observed with laparoscopic approach favoring SH over TH (mean of 13 days versus 5 days, respectively) represented by the single study of *Asgari et al*[26] that evaluated only 45 women and did not specify the criterion used to estimate returning to normal activities (Figure 4d). The heterogeneity between subgroups was 71%.

Secondary outcomes

Persistence of pelvic pain

Number of patients with persistant pelvic pain did not favored a particular technique in general (TH 14.4% versus SH 13.5%; RR 1.02 95%CI [.76, 1.36] p=0.91, i^2=0%, 6 studies, 1041 women) or according to the type of surgical approach[2,20,22–25] (Figure 5a). The heterogeneity between subgroups was 0%.

Cyclical vaginal bleeding

Six studies involving 955 women evaluated this event. The number of patients with cyclical vaginal bleeding was more frequent in the group that had SH (67 out of 472 patients) than TH group (6 out of 483 patients) (14.1% and 1.2% respectively, RR .14 95%CI [0.05, 0.43] p = 0.0006, i^2=39%),[2,20,22,24,25] 34. Subanalysis of the type of surgeries showed that TH patients significantly presented less cyclical bleeding that SH when open abdominal approach was performed (p = 0.02) and heterogeneity of 30%.

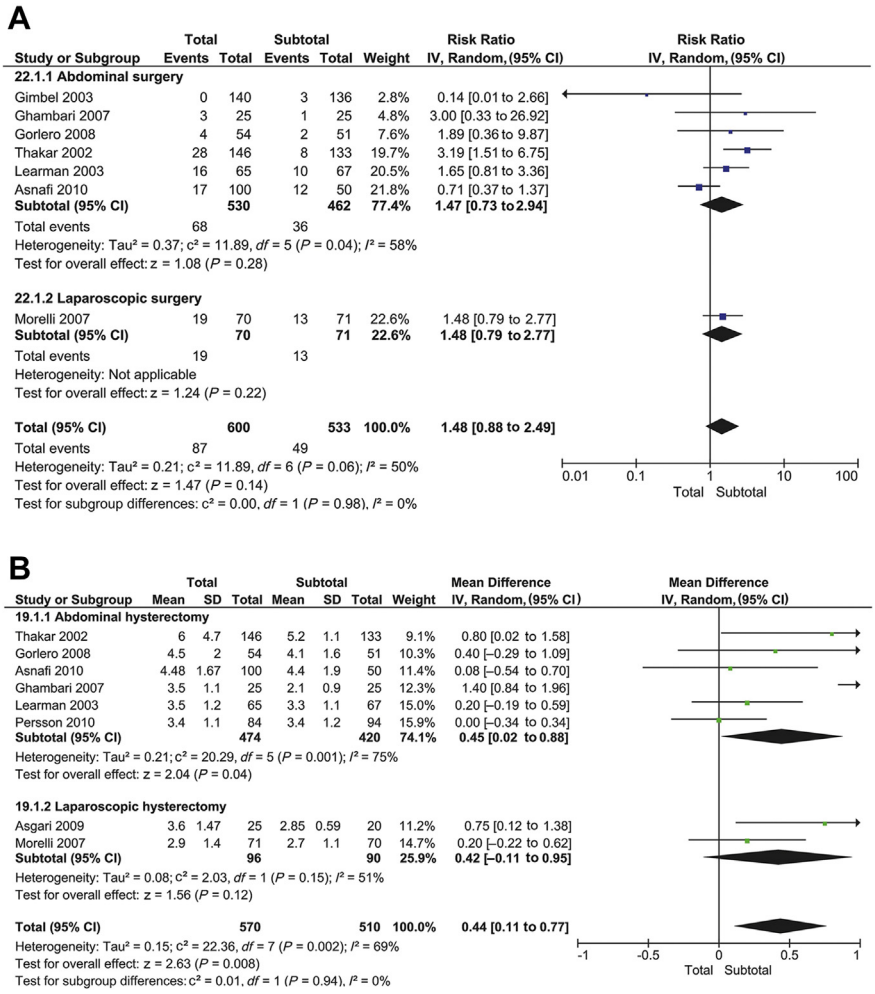

Figure 4. a: Forest plots comparing febrile morbidity between TH and SH. b: Forest plots comparing hospital stay between TH and SH. c: Forest comparing readmission related to surgery between TH and SH. d: Forest plots comparing return to normal activity between TH and SH.

Although not statistically significant, forest plot graphic showed a strong tendency also in favor of TH regarding cyclical bleeding for laparoscopic procedures ($p = 0.05$) (Figure 5b).

Sexual function

Regarding sexual function, limited data were available in the studies. We could analyze dyspareunia and sexual satisfaction rates. For both outcomes, *Thakar et al*[25] used their own non-validated questionnaire and only described the results as numbers of subjects with deep dyspareunia and the ones that reported to have good sexual relationship with partner. *Gimbel et al*[35] used a validated self-administered questionnaire which included the questions "Are you satisfied with your sexual life?" "Do you suffer from pelvic pain?" The authors presented data as number of subjects satisfied with sexual life and number of subjects with dyspareunia. For sexual satisfaction: *Ghanbari et al*[27] do not describe the methodology, only the final numbers are presented as number of subjects satisfied with sexual life.

Pooled data showed that number of patients who had post operative dyspareunia was very similar

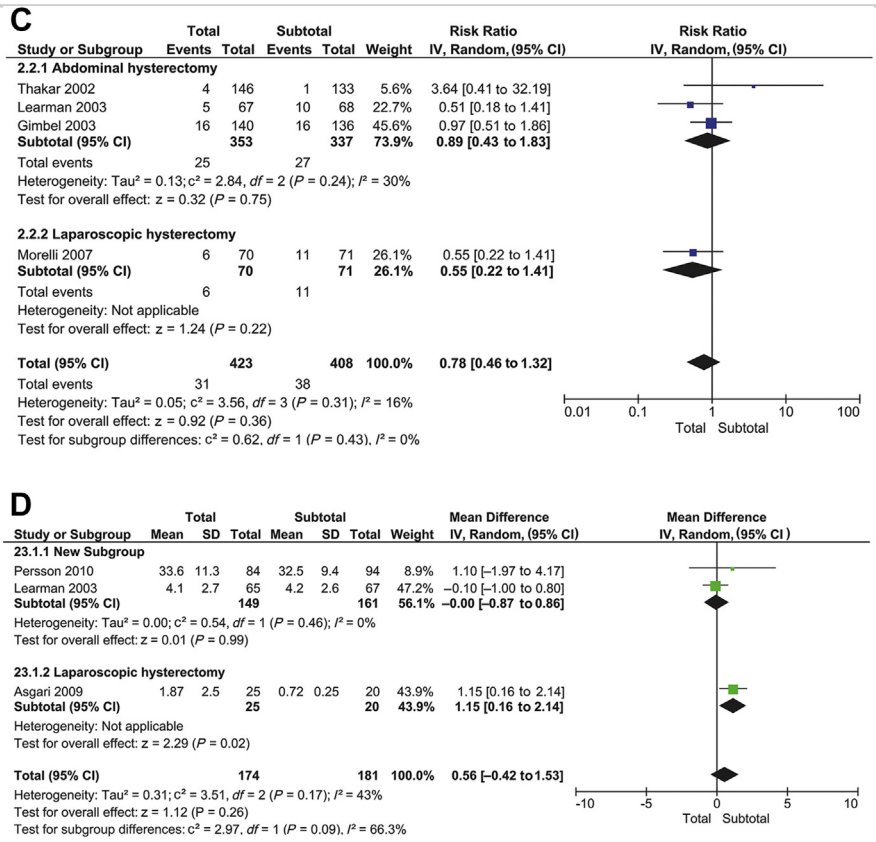

Figure 4. (*continued*).

between TH and SH operations (9% versus 8.3% respectively, RR 1.18 95%CI [0.38, 3.70] p = 0.77, i^2=70% 2 studies, 452 women)[20,25] (Figure 5c).

We also did not find any difference when comparing TH with SH regarding to number of patients that were sexually satisfied after surgery (69% versus 70% respectively, RR .96 95%CI [0.83, 1.12] p = 0.63, i^2=38% 3 studies, 504 women)[20,25] (Figure 6a).

Quality of life

We included manuscripts that evaluated quality of life (physical, mental and quality of life in general) by questionnaires SF-36 or PGWB up to 12 months follow-up, both in which higher score means better outcome. *Thakar et al*[30] did not report data in absolute numbers, but the difference between the baseline and postoperative scores for both techniques.

Pooled data did not detect differences among TH over SH in any domain: physical (MD 0.46 95%CI [-1.28, 2.20] p = 0.61, i^2=0% 3 studies, 652 women)[28,30,31] (Figure 6b), mental (MD 0.59 95%CI [-0.85, 2.02] p = 0.42, i^2=0% 4 studies, 831 women)[28–31] (Figure 6c), and general scores (MD -0.34 95%CI [-0.96, 0.28] p = 0.28, i^2=0%4 studies, 540 women)[2,19,28,30] (Figure 6d). When separating the results according to the surgical approach, no difference was found by removal of the cervix either abdominally or laparoscopically or if the cervix was not removed (Figures 6b, c and d).

DISCUSSION

More evidence has been published in whether the cervix should or not be removed which might be related with SH becoming more and more the preference of women and surgeons in the western world.[36]

This updated systematic review included a larger sample 1,523 women than previous ones[8,10] and 3 more studies.[2,26,27] We found that only estimated blood loss, operative time and hospital stay events favored SH when compared to TH, while cyclical bleeding was more frequent in the SH group.

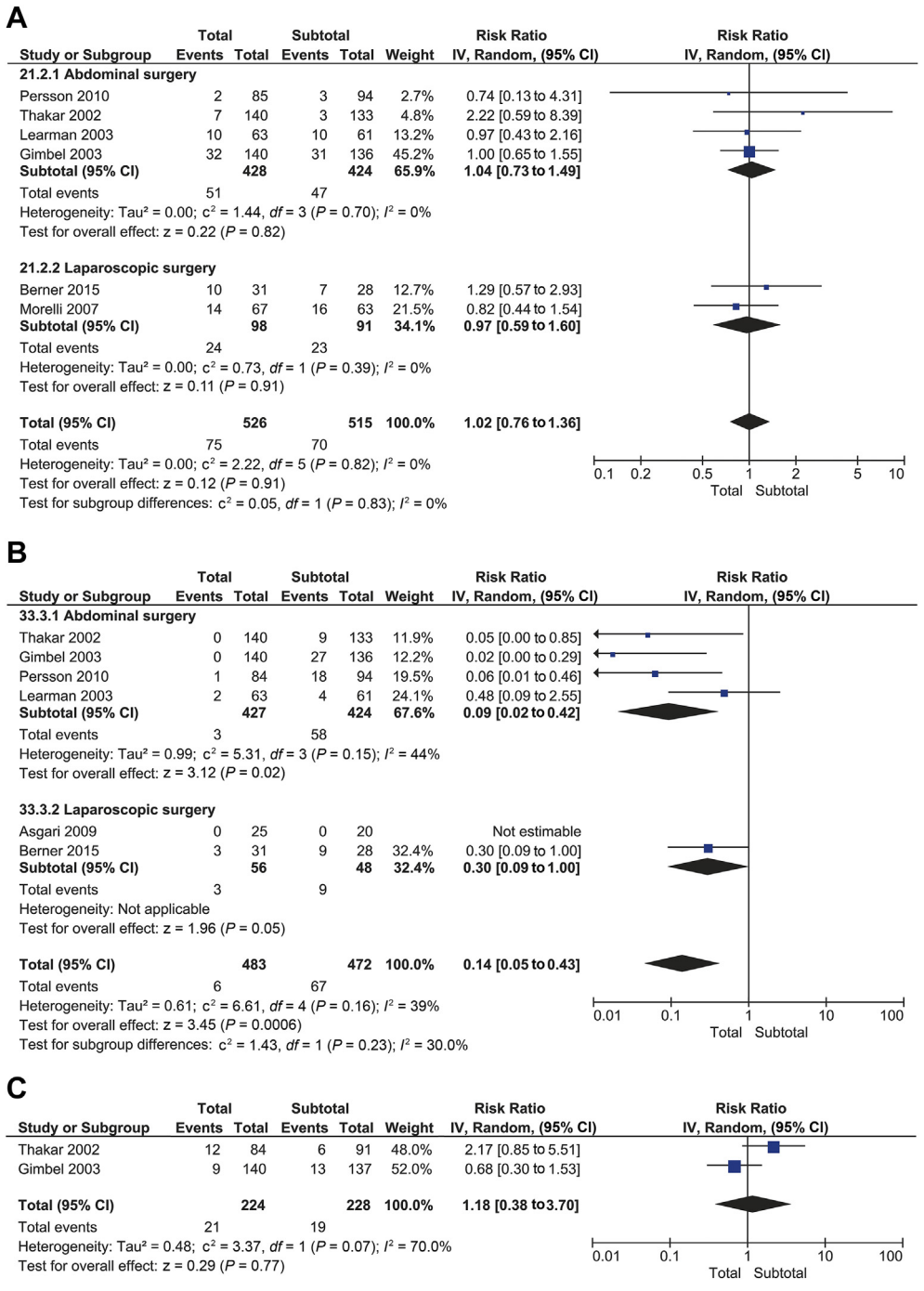

Figure 5. a: Forest plots comparing persistence of pelvic pain between TH and SH. b: Forest plots comparing cyclical vaginal bleeding between TH and SH. c: Forest plots comparing dyspareunia between TH and SH.

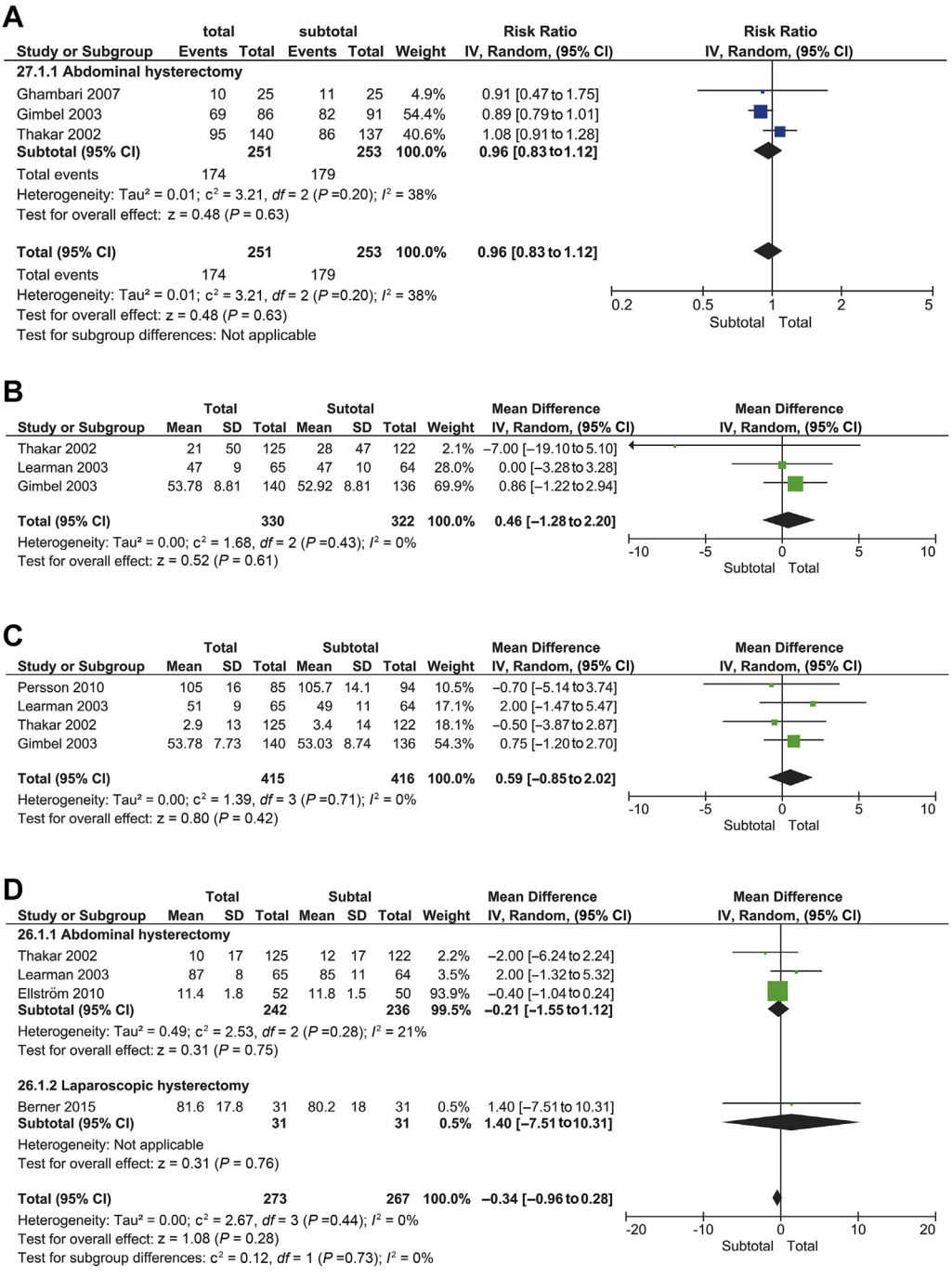

Figure 6. a: Forest plots comparing sexual satisfaction between TH and SH. b: Forest plots comparing physical score between TH and SH. c: Forest plots comparing mental score between TH and SH. d: Forest plots comparing general quality of life between TH and SH.

Importantly, data were originated by the pooled analyses of studies of moderate heterogeneity regarding those variables. The small estimated blood loss difference (around 80 ml) may lose its clinical relevance since no difference was found on the rates of blood transfusion. Shorter intraoperative time is an important outcome usually related to minimally invasive surgeries that may represent a less expensive procedure. We have found that SH had shorter procedure time (12 min) and this can be related to shorter hospital stay (< half of a day), either for open abdominal or laparoscopic approaches. Subtotal hysterectomy also had a shorter return to normal activity (two days), even though this has not reached statistical significance. The clinical validity of the findings on intraoperative time, hospital stay and return to normal activity is questionable. However, a cost-effective analysis would help to establish how relevant are those from the finantial perspective impacting either the health care system burden or the patients work. According to our analysis, return to normal activities was the only outcome influenced by the surgical approach: abdominal or laparoscopic (heterogeneity among the subgroups was 70%), while the other events were not affected by the different techniques. With that, we believe that the combined analyses of both abdominal and laparoscopic approaches are appropriate.

Cyclical vaginal bleeding may be a very concerning event as women who undergo hysterectomy expect to stop menstruating and so this can lead to unnecessary medical investigation and further morbidity. This aspect should be well discussed with the patients specially with the ones having SH. Similar to previous systematic reviews,[8,10] this meta-analysis showed statistical significance toward TH especially due to the results from the open abdominal hysterectomy studies. *Thakar et al.*[25] suggested that if surgeons perform reverse conization during SH whereby excising the cervical epithelium including the transformation zone along with residual endometrium would minimize the risk of bleeding; but there are no further studies on this argument.

Supposedly TH would increase the risk of ureteral lesion over SH during parametrium ligation. However, this meta-analysis did not confirm this assumption.

Potential sexual dysfunction after hysterectomy is a matter of great debate. Recently some observational studies suggested that SH provided better results related to sexual function than TH.[4,5] However, Berlit et. al.[26] found that sexuality was more important to women submitted to SH and this could represent a possible bias due to patient's expectations. The majority of the available data shows that hysterectomy significantly reduces dyspareunia overall[10,30–32,37] althogh Kilkku et al.[27] found statistical difference toward SH. Zobbe et al.[31] found that the best predictor for sexual satisfaction was preoperative sexual satisfaction and that the use of hormonal replacement therapy negatively influenced the sexual life of hysterectomy patients. The TOSH group[22,28] studies also found no statistical differences in sexual function using the MOS sexual problems scale and they described the variety of possible limitations that this type of interventional study can have, either imbalances between groups, lack of masking and difficulties getting informations regarding to sexual activity. Unfortunately, there is no standard to define sexual function and/or satisfaction in most of the studies; only two comparable outcomes (satisfaction with sex and dyspareunia) were possible in this review which failed to find statistical difference between removing or preserving the cervix during hysterectomy.

Similar to the findings of the latest Cochrane review,[10] quality of life scores by SF-36 or PGWB questionnaires did not favor one procedure over another even with the inclusion of one more recent trial.[2] Future RCTs may try to better address subjetive outcomes by using validated tools, especially since patient wellbeing has been important in the decision making process.

Systematic reviews are an excellent tool to increase the power of studies and search for uncommon outcomes; however it also builds up the risk of bias from the included studies which we tried to assess using tools such as the GRADE. Nevertheles some unreported data such as of randomization, blindiness, questionnaires used and its interpretations and type of analysis may lead to biases. In addition, potential biases related to individual characteristics, surgeons' preferences and skills are unavoidable when performing meta-analyses on surgical treatments, preventing two treatments being perfectly controlled. Despite our extensive work to minimize the inconsistencies we can list the main limitations such as the heterogeneity on outcomes that had

statistically relevant results (estimated blood loss, operative time, hospital stay and cyclical bleeding). We recommend careful interpretion on those results. although we believe that this study contributes to the still unsettled debate as to whether to remove or retain the cervix during hysterectomy.

Finally we can summarize the most clinically relevant findings; women that had SH present higher rate of cyclical vaginal bleeding which can influence patient expectations and guarantee unnecessary medical investigations. On the other hand, despite not statistically different, women had a shorter return to normal activities post SH, therefore relevant on patients' choice.

CONCLUSION STATEMENT

We assessed only short term events in our study Long term follow-up may lead to different conclusions. Overall, we cannot state that one surgical approach is better than the other but counseling the patient towards a better decision-making process, especially pointing out that further prospective randomized studies are needed to confirm these findings and that some variables do not have a clear result. In addition, the better intra and perioperative profile in favor of the subtotal hysterectomy may be relevant to the health system from the economical point, subject that should be further addressed to confirm this assumption.

CONFLICT OF INTEREST

The authors report no conflict of interest.

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None.

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APPENDIX A

Search in Pubmed/Medline

1. hysterectomy
2. (((clinical[tiab] AND trial[tiab]) OR "clinical trials as topics"[mesh] OR "clinical trial" [pt] OR random*[tiab] OR "random allocation" [mesh] OR "therapeutic use" [sh]))
3. ((#1 and #2))
4. (subtotal or total)
5. (#3 and #4)
6. (((((((total) AND versus) AND subtotal) OR supracervical) AND hysterectomy)))
7. ((subtotal or supracervical or total))
8. (#5 and #7)
9. ((subtotal or supracervical))
10. total
11. (#5 and #9)
12. (#11 and #10)
13. ((#11 and #10) and berner)
14. ((#11 and #10) and learman)
15. ((#11 and #10) and morelli)
16. ((#11 and #10) and persson)
17. ((#11 and #10) and asnafi)
18. ((#11 and #10) and thakar)
19. ((#11 and #10) and gimbel)
20. ((#11 and #10) and letharby)

Search in Lilacs-Scielo

total OR supracervical OR subtotal OR Histerectomia total [Palavras do resumo] OR histerectomia OR Histerectomia [Palavras do resumo] AND sangramento vaginal cíclico OR sangramento operatório OR tempo de internação OR sangramento requer transfusão OR readmissão[Palavras do Resumo] OR morbidade febril OR lesão trato urinário OR polaciúria AND "ENSAIO CLINICO CONTROLADO ALEATORIO" [Tipo de publicação]

Search in Cochrane CENTRAL

1 hysterectomy.mp.
2 subtotal hysterectomy.mp.
3 total hysterectomy.mp.
4 supracervical hysterectomy.mp.
5 or/1-4
6 pelvic pain.mp.
7 cyclic vaginal bleeding.mp.
8 before discharge events.mp.
9 blood loss during surgery.mp.
10 blood loss requiring transfusion.mp.
11 urinary tract injury.mp.
12 readmission.mp.

13 febrile morbiditymp.
14 Return to normal activity.mp.
15 or/6-14
16.5 and 15
17 Limit 16 to year="1950-Current"

Search in SCOPUS

((((((total) AND versus) AND subtotal) OR supracervical) AND hysterectomy))

Search in Clinicaltrials.gov

Conditions: benign uterine
Study type: interventional
Recruitment status: completed
Age group: adults
Sex: female
Intervention: hysterectomy

AAGL

Hysterectomy

IUGA

Hysterectomy

ICS

Hysterectomy

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