Sarem Journal of Medical Research. Volume 10, Issue 4, Winter 2026: 209- 223

Clinical Outcomes and Complications of Extraperitoneal Caesarean Section: A Systematic Review and Network Meta-Analysis

ARTICLE INFO

DOI: 1052547/sjrm.10.4.7

Article Type

Meta-Analysis

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Received: 11 January 2026
Accepted: 14 February 2026
e Published: 12 March 2026

Article History

ABSTRACT

Background: Various cesarean delivery approaches have been developed to accelerate postpartum recovery and reduce perioperative and postoperative complications. The aim of this study was to compare the clinical outcomes and complications of ECS and TCS for cesarean delivery. Additionally, we investigated different techniques employed in ECS itself to find the best method of CS.

Methods: A PRISMA-guided systematic search was conducted on electronic databases to identify studies from 1945 to 2023. Studies comparing extraperitoneal cesarean section (ECS) and transperitoneal cesarean section (TCS) for cesarean delivery constituted the included population. Observational and RCT studies were included, with a focus on surgical outcomes, complications, and postoperative recovery. The quality of manuscripts was assessed using the CONSORT and Newcastle-Ottawa scales. Hedges' g standardized mean differences (SMD) and Mantel-Haenszel risk ratio (RR) were used for data synthesis. Network meta-analysis was also performed to compare ECS techniques.

Results: A systematic review and meta-analysis of 698 potential studies on extraperitoneal Caesarean sections (ECS) and transperitoneal cesarean sections (TCS) found no significant difference in total operation time. However, the French AmbUlatory Cesarean Section (FAUCS) method showed longer operation times, while classical paravesical ECS showed shorter times. ECS patients experienced greater blood loss but no significant difference in hemoglobin change. ECS patients were associated with a higher risk of intra-operative vomiting and nausea, while TCS patients reported higher post-operative pain levels. ECS patients had a faster recovery of gastrointestinal function, but the risk of urinary tract infection was comparable between ECS and TCS. When considering RCTs, CONSORT indicated variations in the completeness and quality of reporting in these trials. For the observational studies, the majority received scores of 8 or 9, demonstrating a consistent and relatively high level of methodological quality in these study designs.

Conclusions: This update provides reproductive clinicians and scientists with valuable insights into the clinical outcomes and complications associated with extraperitoneal cesarean sections. By comparing different approaches and their effects on surgical outcomes, pain management, and complications, this study informs clinical practice, helping clinicians make more informed decisions and potentially improve patient care.

Keywords: Cesarean; Extraperitoneal; Meta-analysis; Systematic review

[DOI: DOI: 1052547/sjrm.10.4.7]

Introduction

Cesarean delivery is one of the most common obstetric operations. The rate of this common operation is on an increasing trend worldwide [1]. Cesarean delivery carries a higher risk of complications for both mothers and newborns compared to vaginal delivery, necessitating additional care and incurring higher costs [2]. Various complications and postoperative pain may arise following cesarean surgeries performed through different techniques, prompting obstetricians to seek more effective surgical methods. Various cesarean delivery approaches have been developed to expedite postpartum recovery and minimize perioperative and postoperative complications. Transperitoneal CS (TCS), such as the Misgav Ladach TCS (also known as the Joel-Cohen technique), is widely used in many countries. However, the puerpera often experiences severe postoperative pain, affecting the care of themselves or the newborns, the mother-infant relationship, and lactation ability. Postoperative adhesions resulting from TCS [3] may complicate future pelvic surgeries and adversely affect fertility [4]. Another cesarean method is extraperitoneal CS (ECS), a type of surgery for infant delivery through an incision in the lower abdomen without entering the peritoneal cavity. Compared to TCS, this type of operation comes with the advantage of having a smaller chance of abdominal cavity infection and being able to avoid postoperative adhesion of the abdominal and pelvic cavities [5].Other advantages of ECS over TCS include no bowel handling, no chances of losing a surgical mop into the peritoneal cavity [6], and a shorter recovery time, with 90% of pregnant patients reporting discharge within 1 day after surgery [7]. ECS reportedly performed better than TCS with respect to intraoperative nausea, postoperative pain, and analgesic requirements [8]. ECS was proposed in the pre-antibiotic era, and the available clinical reports were primarily published in the second half of the 20th century. To reduce the severe morbidity of TCS in the pre-antibiotic era, an extra-peritoneal approach to CS was devised. The technique of ECS was proposed in 1824 by Philip Physick by separating the peritoneum from the bladder's dome to expose the lower uterine segment [9]. Fritz Frank performed the first successful ECS in 1907 [9]. However, this approach declined after the 1950s, once the antibiotic era started. Moreover, it has never been popular among obstetricians because of the delay in delivery of the fetus, safety, feasibility of surgery, and high likelihood of unintentional perforation of the peritoneum [10]. Conversely, recent research has focused on comparing clinical outcomes and complications between ECS and TCS [11-13]. We hereby aim to assess and compare ECS and TCS in order to find the difference between techniques in regards to surgical outcomes as well as complication rates. Additionally, we investigated different techniques employed in ECS itself to find the most effective method of CS. Our findings could help clinicians make better choices for the CS technique based on their geographical location and the antibiotic resistance status of the region.

Methods

We conducted this systematic review and meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [14]. This review followed a predetermined methodology that was recorded in the prospective register of systematic reviews (PROSPERO) (CRD42023422398).

Eligibility criteria, information sources, search strategy

The following inclusion criteria were used to find eligible studies:
1) Participants: Patients undergoing cesarean delivery; 2) Exposure: Patients undergoing extraperitoneal cesarean section; 3) Comparison: Patients undergoing intraperitoneal or other types of cesarean delivery; 4) Outcome: Surgical outcomes and clinical complications of cesarean delivery; 5) Types of studies: Observational and interventional studies were included. The following criteria for exclusion were used: 1) insufficient data to estimate risk ratio (RR) or standardized mean difference (SMD); 2) Reviews, technique articles, case reports, conference abstracts, animal studies, cadaver studies, and expert-opinion studies; 3) Studies including patients without undergoing extraperitoneal cesarean section; 4) Studies with no control groups, such as the intraperitoneal cesarean delivery group; 4) Studies including patients with abnormal placentation, abruption, cord prolapse, and previous non-cesarean major abdominal surgery.
Two reviewers (VS, AA) independently performed a systematic search through PubMed, Scopus, and Web of Science (WoS) databases (until May 2023) on the comparison of extra-peritoneal cesarean section with trans-peritoneal cesarean section using the terms listed in table 1. The leading keywords were: "extraperiton*"[tiab] AND "cesarean section"[Mesh]. Other resources, related gray literature, publications' reference lists, and related principal journals were also searched for additional publications.

Table 1. Search strategy for each database

Database	Search Query	Results
PubMed	("extraperiton*"[tiab] OR "extra periton*"[tiab] OR "extra-periton*"[tiab]) AND ("cesarean section"[Mesh] OR "cesarean*"[tiab] OR "CS"[tiab] OR "Cesarean deliver*"[tiab] OR "CD"[tiab] OR "C-section"[tiab] OR "C section"[tiab])	177
Web of Science	TS= ("extraperiton*" OR "extra periton*" OR "extra-periton*") AND TS= ("cesarean section" OR "cesarean*" OR "CS" OR "Cesarean deliver*" OR "CD" OR "C-section" OR "C section")	52
Scopus	(TITLE-ABS-KEY("extraperiton*" OR "extra periton*" OR "extra-periton*")) AND (TITLE-ABS-KEY("cesarean section" OR "cesarean*" OR "CS" OR "Cesarean deliver*" OR "CD" OR "C-section" OR "C section"))	246

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Embase	("extraperiton*":ti,ab,kw OR "extra periton*":ti,ab,kw OR "extra-periton*":ti,ab,kw) AND ('cesarean section'/exp OR "cesarean*":ti,ab,kw OR "CS":ti,ab,kw OR "Cesarean deliver*":ti,ab,kw OR "CD":ti,ab,kw OR "C-section":ti,ab,kw OR "C section":ti,ab,kw)

Study selection

Studies were screened using Rayyan (https: //www.rayyan.ai), a web-based software for systematic reviewing. Two reviewers (VS, AA) evaluated each study independently, screening the title and abstract, removing duplicates, assessing the full text. Eligible studies were selected as per inclusion-exclusion criteria. Conflicts that may arise between reviewers were resolved with the help of consensus meetings presided over by the third author (PM).

Data extraction

After reading through all the full texts, two researchers (VS, AA) independently filled in a pre-made Excel sheet with the below information. The collected data consisted of: authors, year of publication, location of study, study design, level of evidence, sample size, gender, mean age of patients, BMI, co-morbidities, operation duration, blood loss, pain score, infection, and intraoperative nausea. Conflict was assessed by the third reviewer (PM). Different ECS techniques were also extracted, including classical paravesical, FAUCS (French AmbUlatory Cesarean Section), Latzko, and MECS (modified ECS). In the classical paravesical, the incision is made in the lower abdomen, parallel to the inguinal ligament and slightly medial to the anterior superior iliac spine. The dissection is carried out between the rectus muscle and the lateral border of the rectus sheath, entering the space of Retzius and providing good exposure to the lower uterine segment [7,8,12,15-21]. FAUCS is a technique designed to minimize postoperative pain and facilitate early ambulation and discharge. It involves making a small incision in the lower abdomen, typically at or just above the pubic hairline. The incision is extended laterally in a curvilinear fashion, allowing access to the lower uterine segment [4,11,13]. The Latzko technique involves making an incision in the lower abdomen, similar to a Pfannenstiel incision but slightly higher. The incision is typically made transversely, just above the pubic hairline. The rectus sheath is opened, and the rectus muscles are separated in the midline to access the lower uterine segment. This approach provides good exposure and is commonly used in cases where a traditional transperitoneal cesarean section may not be feasible or desirable [22,23]. MECS is a variation of the extraperitoneal cesarean section technique that aims to minimize postoperative adhesions and complications. In MECS, the incision is made in the lower abdomen, typically just above the pubic hairline. The rectus sheath is opened, and the rectus muscles are separated in the midline. However, in MECS, special care is taken to avoid entering the peritoneal cavity. Instead, the incision is extended through the rectus sheath and anterior rectus fascia, allowing access to the lower uterine segment while minimizing contact with intra-abdominal structures [24].

Assessment of risk of bias

We used the Newcastle-Ottawa Scale (NOS) and CONSORT protocol to assess the quality of observational studies. NOS was developed to assess the quality of observational studies, including case-control and cohort studies, with its design, content, and ease of use. The guideline consists of three categories: 1) selection of study groups (four points); 2) comparability of groups (two points); and 3) ascertainment of exposure and outcomes (three points) [25]. The most rigorous studies score up to 1 star per component. The NOS covers scores from 0 to 9 (selection = 4, comparability = 2, and outcome = 3). For interpretability, NOS scores are categorized as: 7–9 stars = high quality, 4–6 stars = moderate quality, and <4 stars = low quality [26]. As for the quality of included randomized controlled trials (RCTs), we utilized the CONSORT 2010 statement, which contains six domains: title and abstract, introduction, method, results, discussion, and other information (registry number, full trial protocol, sources of funding). The maximum possible score on the CONSORT scale that can be given to an article is 37, scores ≥25 indicate high-quality reporting, 13–24 moderate, and ≤12 low quality [27].

Data synthesis

Stata 17.0 was used to conduct the data synthesis. (ver. 17.0; StataCorp LP, College Station, TX, USA). Hedges' g standardized mean differences (SMD) was used to evaluate continuous outcomes [28]. The effect estimate for all categorical data was chosen to be the risk ratio (RR) with associated 95% confidence intervals (CI), generated using the Mantel-Haenszel method. A fixed-effect model or a random-effects model was used to pool study-specific effect sizes depending on the degree of variability. With the Q-test and I2, statistical heterogeneity was evaluated. I2 values of 25, 50, and 75%, respectively, were considered to represent low, moderate, and high heterogeneity [29]. A fixed effect model was applied if P>0.1 and I2<50%; otherwise, a random-effect model was applied. Egger's test was run to evaluate the publication bias [30]. A value of P<0.05 was regarded as indicating statistical significance for all data analyses, with the exception of heterogeneity, and all tests were two-sided. To understand how robust the overall results are for certain studies, a sensitivity analysis using leave-one-out analysis was conducted. The complications section of our results was categorized into acute (intra-operative vomiting and nausea, post-operative visual analog scale (VAS)) and sub-chronic (time until the first gas passage and the

[DOI: DOI: 1052547/sjrm.10.4.7]

risk of urinary tract infection (UTI)) for better comprehension.

Network meta-analysis is achieved by combining direct and indirect evidence. Direct evidence refers to evidence obtained directly from randomized control trials, and indirect evidence refers to that obtained through one or more common comparators [31]. The network meta-analysis (NMA) was performed using Stata 17.0. The mean and SD were used to compare the effects of different methods of CS. The relative effect on multiple intervention comparisons was estimated using a random-effects network meta-analysis. The surface under the cumulative ranking curve (SUCRA) value is the probability each treatment has of being among the best of those in the network, with larger values representing higher ranking probabilities. The SUCRA value and cumulative ranking plots were used to calculate the ranking probabilities of each intervention. Consistency, one of the assumptions of NMA, is the statistical agreement between the direct and indirect comparisons. It is the statistical manifestation of transitivity in the data [31].

Results

Study selection

A comprehensive search of various databases initially yielded 698 potential studies. After removing 237 duplicates, the remaining 461 records underwent title and abstract screening, resulting in the exclusion of 417 studies. Subsequently, 44 studies were subjected to full-text assessment, of which 17 met the inclusion criteria and were included in this systematic review. Among these, 14 studies entered meta-analysis, with 3 failing to report adequate data (Figure 1). No other studies from the hand search were considered eligible based on the review of the reference lists of the pertinent articles.

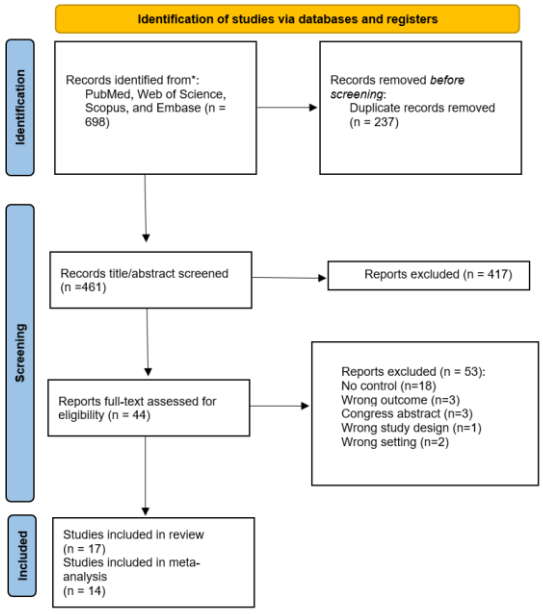

Figure 1. PRISMA flow diagram

Study characteristics

The included studies were conducted in diverse geographic locations, including the USA[20,22,23,32], India[15,16,24], China [12,22], Turkey [8,17-19], Tunisia [4,11], Israeli [13], and Austria [7]. The study designs encompassed RCT[7,8,11,13,15,16,19-21,23], retrospective cohort [4,12,32], observational [22,241], and case-control [17,18].. In total, 1,492 patients underwent ECS as the case group, while 1,730 patients underwent TCS as the control group. The mean age at the time of surgery was 28.2 years (range, 24-33.9 years), and the mean body mass index (BMI) was 28.1 kg/m² (range, 21.7-32.08 kg/m²). The ECS approaches employed in the studies included classical paravesical ECS (n = 809 patients) [7,8,12,15-21], FAUCS (n = 168 patients) [4,11,13] , , Latzko (n = 421) [22,23], and MECS (modified ECS) (n = 91 patients) [24]. A comprehensive summary of demographic information is available in (Table 2).

Table 2. Baseline characteristics of the included studies

Study	Groups	N	Country	Study design	Age	BMI	ECS	Gestational	Gravidity	Parity	NOS	CONSORT
Ji2022	ECS	229	China	Retrospective	31.33±3.66	28.81±3.82	Classical	39.43±3.66	NA	NA	9	NA

[DOI: DOI: 1052547/sjrm.10.4.7]

Wallace1983_A		Tappauf2013		Yapca2018		
TCS	ECS	TCS	ECS	TCS	ECS	TCS
36	50	27	27	105	105	232
USA		Austria		Turkey		
RCT		RCT		RCT		
25.36±7.05	24.24±6.07	31.4±7.2	29.9±4.9	29±6	28±6	30.79±4.18
NA	NA	24.2±3.9	22.4±2.4	30±6	29±5	28.97±3.82
Classical paravesical ECS (n = 91)		Classical paravesical ECS (n = 27)		Classical paravesical ECS (n = 105)		
40.31±2.09	40.5±225	39.2±0.9	38.8±1.2	37±4.5	37±2.75	30.79±4.18
NA	NA	NA	NA	46 primigravid/44 multigravid	48 primigravid/46 multigravid	NA
26 nullipar/10multipar	40 nullipar/10multipar	13 nulliipar/14multipar	16 nulIipar/11multipar	NA	NA	NA
NA		NA		NA		
15		23		24		

Sagi2023		Vaswani2020		Shinde2012		Wallace1983_C		Wallace1983_B	
TCS	ECS	TCS	ECS	TCS	ECS	TCS	ECS	TCS	ECS
58	58	30	30	100	91	36	16	36	25
Israeli		India		India					
RCT		RCT		Observational					
33.6±4.6	33.9±6	NA	NA	24±3		25.36±7.05	24.69±5.13	25.36±7.05	24.8±5.89
29.9±4	29.5±4.5	NA	NA	NA	NA	NA	NA	NA	NA
FAUCS (n = 58)		Classical paravesical ECS (n = 30)		MECS (n = 91)					
38.7±0.7	38.7±0.8	NA	NA	NA	NA	40.31±2.09	40.19±2.14	40.31±2.09	39.32±3.53
NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
NA	NA	NA	NA	NA	NA	26 nullipar/26multipar	11 nullipar/5multipar	26 nullipar/10multipar	19 nullipar/6multipar
NA		NA		8					
25		19		NA					

Dimassi2021	
TCS	ECS
50	50
Tunisia	
RCT	
33.86±0.75	32.8±0.77
31.79±0.61	30.42±0.55
FAUCS (n = 50)	
39.08±0.1	30.14±0.1
2.5 ± 0.5	2.5 ± 2
2±1	2±0.97
NA	
25	

Dimassi2019	
TCS	ECS
52	60
Tunisia	
Retrospective Cohort	
32.06±5.6	32.73±5.5
32±4.88	32.08±4.43
FAUCS (n = 60)	
NA	NA
NA	NA
2±0.87	NA
9	
NA	

Cosgrove 1946	
TCS	ECS
510	127
USA	
Retrospective Cohort	
NA	NA
NA	NA
Classical paravesical ECS (n = 127)	
NA	NA
NA	NA
NA	
NA	

ATHERTON 1954	
TCS	ECS
68	**75**
USA	
Observational	
14-42	14-41
NA	NA
Latzco (n = 75)	
NA	NA
NA	NA
59nullipar/16multipar	42 nullipar/59multipar
NA	
NA	

Senturk2018	
TCS	ECS
25	25
Turkey	
RCT	
NA	NA
30.23±4.13	30.01±4.4
Classical paravesical ECS (n = 25)	
38.1±1.72	38.9±0.89
NA	NA
NA	NA
NA	
9	

Ying2018	
TCS	ECS
31	31
China	
RCT	
27.1±4.1	26.3±4.9
22.4±2.4	21.7±3.8
Classical paravesical ECS (n = 31)	
38.9±1.6	39.3±1.4
22 primigravid	20 primigravid
NA	NA
NA	
19	

Bebincy 2017	
TCS	ECS
80	80
India	
RCT	
NA	NA
NA	NA
Classical paravesical ECS	
NA	NA
NA	NA
NA	NA
NA	
NA	

Yeslilbas2017	
TCS	ECS
34	34
Turkey	
Case-control	
27.2±5.9	27.4±5.6
NA	NA
Classical paravesical ECS (n = 34)	
39±1.6	39.5±0.8
21 primigravid	18 primigravid
21nullipar/13multip	18nullipar/16multip
8	
18	

Karaaslan2020	
TCS	ECS
30	30
Turkey	
Case-control	
25.17±3.39	24.83±3.38
26.3±2.79	26.57±3.08
Classical paravesical ECS (n = 30)	
37.07±1.68	37.47±1.59
NA	NA
NA	1.4±0.6
5	
NA	

Hanson1984	
TCS	ECS
190	346
USA	
RCT	
28	26.5
NA	NA
Latzco (n = 346)	
NA	NA
NA	NA
0.5±0.7	2±1.2
NA	
11	

Abbreviations: N, number; BMI, body mass index; ECS, extraperitoneal cesarean; NOS, Newcastle-Ottawa scale; Consort, Consolidated Standards of Reporting Trials; RCT, Randomized Clinical Trial; TCS, Transperitoneal cesarean; NA, Not Available; FAUCS, French Ambulatory cesarean section;

Risk of bias in included studies

To assess the risk of bias in the included studies, the CONSORT and Newcastle-Ottawa Scale (NOS) were employed. Of the RCTs, the CONSORT score ranged from 9 [19] to 25 [11,13] out of 25. Of retrospective cohort [4,12,32], observational [22,24], and case-control [17,18] studies all received scores of 8 and 9, except for one study receiving 5 [18]. (Table 2).

As for publication bias, we ran the regression-based Egger test for small-study effects on RCTs reporting the operation time (the outcome with the highest number of studies) and found no publication bias (P=0.51).

Synthesis of results

Findings of qualitative synthesis

Regarding studies with cohort design, insufficient data prevented the possibility of meta-analysis except for operation time (SMD[95%CI]=-0.50[-0.69,-0.32]; I2=99%; P=0.00) being longer in TCS patients (Figure 2).

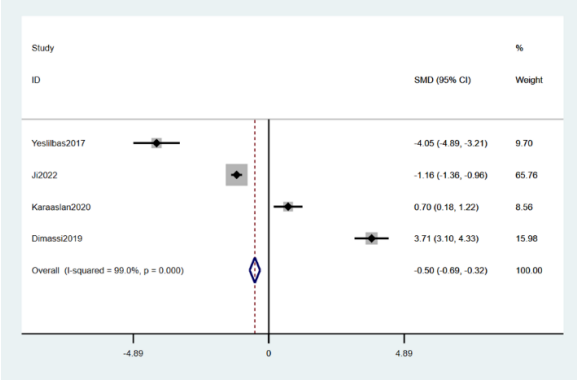

Figure 2. Forest plot for operation time of ECS vs. TCS among cohort studies

Yesilbas et al. [17] found considerably increased intra-operative rates of nausea and vomiting in patients undergoing TCS. Superior postoperative results were demonstrated by ECS patients, who had a quicker recovery of gastrointestinal function and fewer noticeable hemoglobin alterations. Furthermore, TCS patients needed more opioid analgesics to manage their pain, which may indicate that they had more discomfort from this approach. Dimassi et al. [4,11] highlighted differences in ECS techniques. Specifically, FAUCS has a longer incision-to-delivery time than Misgav Ladach (Joel-Cohen–based) transperitoneal cesarean technique. Overall, (Table 3) provides a summary of the qualitative synthesis comparing various approaches to cesarean deliveries, including surgery length, complications, and pain control techniques.

Table 3. Clinical outcomes in ECS vs. TCS groups of the included studies

Study	Groups	Incision-to -delivery time (min)	Total operation time (min)	Intraoperative Blood Loss (ml)	Change in Hb (mg/dl)	Infection	Nausea and vomiting	VAS pain	Time until gas passage(hour)
Ji2022	ECS	NA	40.01±8.89	512.47±154.29	NA	14puerperal	NA	1.85±1.26	1.18±0.44
	TCS	NA	51.51±10.81	491.92±202.24	NA	23puerperal	NA	2.09±1.34	1.21±0.43
Yapca2018	ECS	3.9±1.3	26.9±17.2-41.3	NA	2±1	NA	4	3±1_9	8±4
	TCS	4.2±1.6	30±19.9-75.8	NA	2±1	NA	7	5±1_8	13±4
Tappauf2013	ECS	NA	29±3.9	NA	0.75±0.72	2UTI	NA	NA	NA
	TCS	NA	35±10.5	NA	1.05±0.85	3UTI	NA	NA	NA

[DOI: DOI: 1052547/sjrm.10.4.7]

Sagi2023		Vaswani2020		Shinde2012		Wallace1983_C		Wallace1983_B		Wallace1983_A	
TCS	ECS	TCS	ECS	TCS	ECS	TCS	ECS	TCS	ECS	TCS	ECS
22.8±13.1	29.3±18.5	NA	NA	3.1±0.75	6±1.03	8.39±4.18	8.94±2.77	8.39±4.18	9.56±4.38	8.39±4.18	9.29±3.58
43.7±11.2	54.4±11.3	NA	NA	NA	NA	53.83±25.45	36.31±8.4	53.83±25.45	40.68±19.18	53.83±25.45	38.47±13.42
637.1±153.6	697.4±226	490	476	NA	NA	NA	NA	NA	NA	NA	NA
0.7637.1±153.60.8	1.1697.4±2261.6	490	476	NA	NA	NA	NA	NA	NA	NA	NA
NA	NA	NA	NA	NA	NA	3wound/1UTI	1UTI	3wound/1UTI	2wound/1UTI	3wound/1UTI	2wound/2UTI
NA	NA	10	0	NA	NA	NA	NA	NA	NA	NA	NA
NA	NA	6.86±	4.13±	NA	NA	NA	NA	NA	NA	NA	NA
NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Karaaslan2020		Hanson1984		Dimassi2021		Dimassi2019		Cosgrove 1946		ATHERTON 1954		Senturk2018	
TCS	ECS	TCS	ECS	TCS	ECS	TCS	ECS	TCS	ECS	TCS	ECS	TCS	ECS
NA	NA	6	5.5	NA	NA	6±1.7	13±3.6	NA	NA	NA	NA	3.04±1.4	7.6±2.1
25.5±4.3	28.27±3.6	34	23	38.38±2.24	43.31±7.34	35±30-40	50±40-60	NA	NA	NA	61±	21.48±3.45	26.96±7.92
NA	NA	NA	NA	520±58	536±50	213±87	199±143	NA	NA	NA	NA	NA	NA
11.95±1.45	11.74±1.26	NA	NA	520±58	536±50	213±87	199±143	NA	NA	NA	NA	1.27±0.59	1.5±0.91
NA	NA	1UTI	5/6UTI	NA	NA	NA	NA	NA	NA	2wound	19wound/1 pelvic abscess	NA	NA
15	4	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
NA	NA	NA	NA	2.56±0.36	1.1±0.18	4±3.7-5	3±2_5	NA	NA	NA	NA	3±1_7	1±0_4
NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	19.24±9.6	11.96±5.48

Yeslilbas2017	TCS	2.1±0.37	35.5±3.6	NA	1.09±0.24	NA	17	NA	27.2±3.2
	ECS	2±0.12	23.1±2.4	NA	0.67±0.13	NA	0	NA	11.2±1.5
Bebincy 2017	TCS	2.05±	26±	NA	NA	6	NA	7.06±	NA
	ECS	4.57±	29.48 +	NA	NA	0	NA	4.28±	NA
Ying2018	TCS	NA	31.7±5.5	NA	1.3±0.6	NA	3.5	3.72±2.34	NA
	ECS	NA	30.1±2.7	NA	1±0.5	NA	0	3±2.29	NA
								-3.82	

Abbreviations: Min, minute; mL, milliliter; Hb, Hemoglobin; VAS, Visual analog scale; NA, Not Available; UTI, Urinary Tract infection;

Findings of quantitative synthesis

Surgical Outcomes

A meta-analysis was conducted to compare the total operation time between ECS and TCS, revealing no significant difference (Standardized Mean Difference [SMD] [95% CI] = -0.08 [-0.58, 0.41]; I^2 = 90.9%; p = 0.74). However, when stratified by ECS approach (classical paravesical ECS, FAUCS, Latzko, and MECS), FAUCS showed a significantly longer operation time (SMD [95% CI] = 0.93 [0.65, 1.21]; I^2 = 0%; p = 0.00) compared to TCS, whereas classical paravesical ECS demonstrated shorter operation times compared to TCS (SMD [95% CI] = -0.39 [-0.76, -0.01]; I^2 = 77.2%; p = 0.04) **(**Figure 4**).**

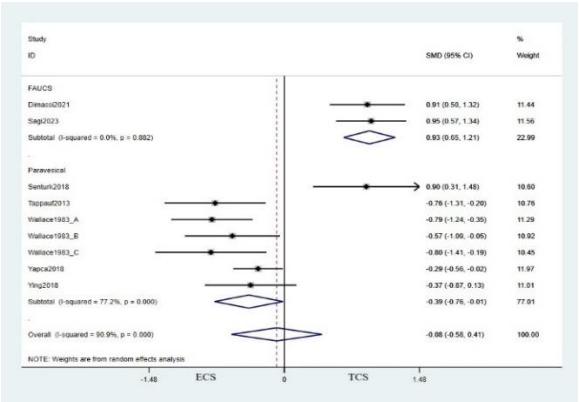

Figure 3. Forest plot for operation time of ECS vs. TCS among RCT studies

After the exclusion of Senturk et al [19], as a source of heterogeneity, from the classical paravesical ECS subgroup, significantly shorter operation times were obtained in the ECS group (SMD [95% CI] = -0.53 [-0.73, -0.32]; I^2 = 18.4%; p = 0.00) **(**Figure 4A**)**. Our analysis highlighted that the incision-to-delivery time was a crucial factor contributing to longer operation times in ECS patients compared to TCS (SMD [95% CI] = 1.24 [0.29, 2.19]; I^2 = 97.1%; p = 0.01) **(**Figure 4B**)**. After excluding Senturk et al. [19], the difference in incision-to-delivery time between ECS and TCS was no longer significant (SMD [95% CI] = 0.05 [-0.22, 0.32]; I^2 = 35.9%; p = 0.71) **(**Figure 4C**).**

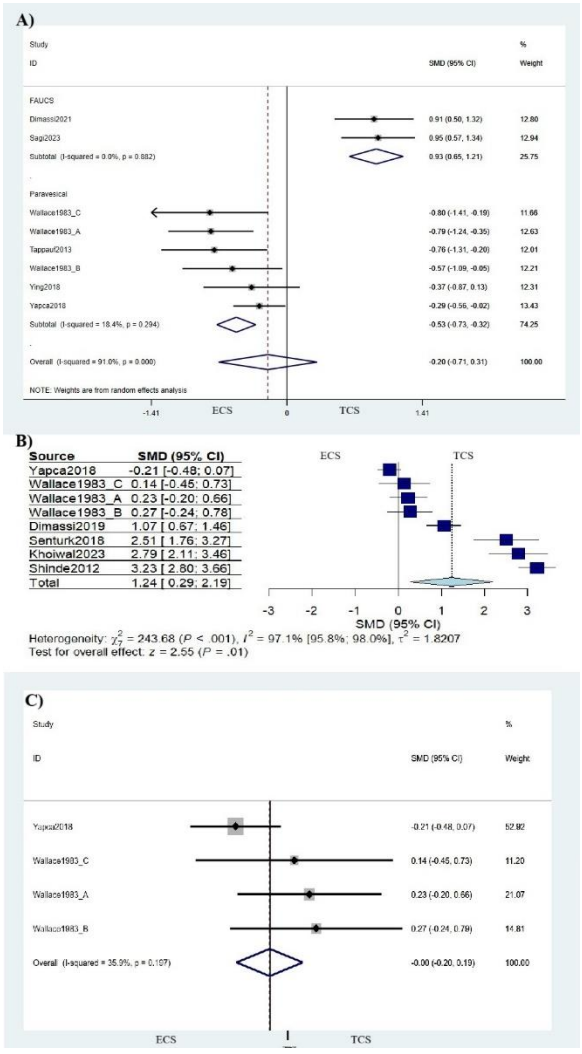

Figure 4. A) Forest plot for operation time of ECS vs. TCS among RCT studies after the elimination of Senturk et al. B) Forest plot for incision-to-delivery time of ECS vs. TCS C) Forest plot for incision-to-delivery time of ECS vs. TCS after the elimination of Senturk et al.

A network meta-analysis was conducted on the operation time of classical paravesical ECS, FAUCS ECS, and TCS methods (Figure 5). Our synthesis

[DOI: DOI: 1052547/sjrm.10.4.7]

revealed that TCS had the highest probability of being the most prolonged CS technique (SUCRA=98.5), followed by FAUCS (SUCRA=47.8). We illustrated that classical paravesical ECS is attributed to the lowest probability of extended operation time (SUCRA=3.7) (Figure 6).

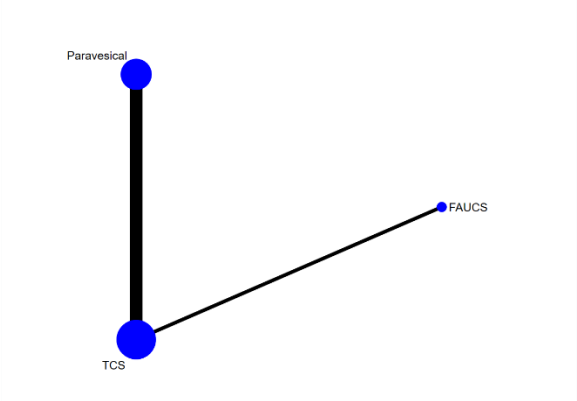

Figure 5. Network meta-analysis of eligible comparisons for operation time of ECS vs. TCS among RCT studies

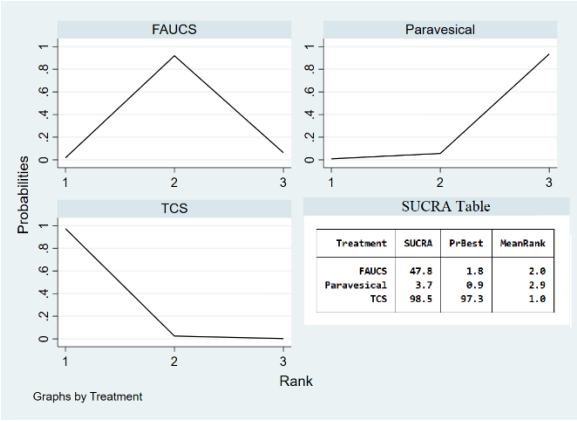

Figure 6. The surface under the cumulative ranking curve (SUCRA) ranking chart and table for operation time of ECS vs. TCS among RCT studies

Additionally, ECS patients experienced greater blood loss than TCS patients (SMD [95% CI] = 0.30 [0.04, 0.57]; I^2 = 0%; p = 0.03) (Figure 7). Although blood loss theoretically affects hemoglobin levels, the analysis demonstrated no significant difference in hemoglobin change between ECS and TCS (SMD [95% CI] = -0.04 [-0.34, 0.27]; I^2 = 61.2%; p = 0.81) **(**Figure 8). After excluding Senturk et al. in subgroup analysis [19], FAUCS patients showed a greater hemoglobin change in ECS compared to TCS. However, classical paravesical ECS might be associated with less hemoglobin change, although neither reached statistical significance (Figure 9).

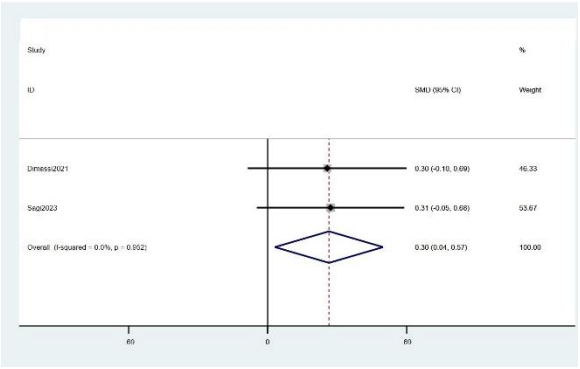

Figure 7. Forest plot for blood loss of ECS vs. TCS

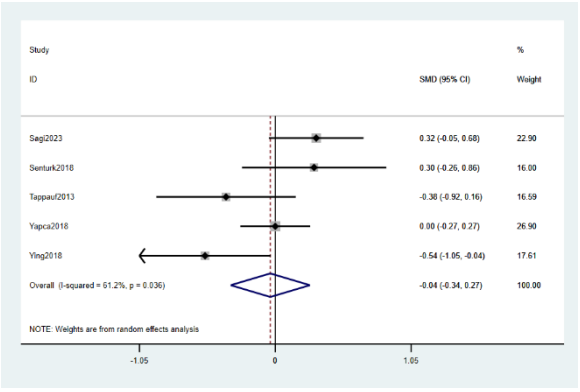

Figure 8. Forest plot for hemoglobin change of ECS vs. TCS

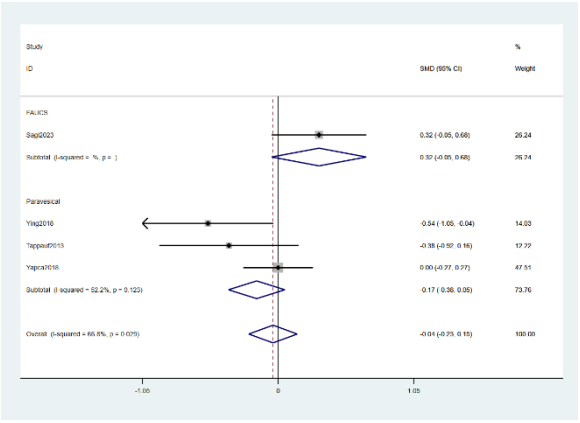

Figure 9. Forest plot for hemoglobin change of ECS vs. TCS after the elimination of Senturk et al.

Complications

Complications were categorized into acute and sub-chronic subsets. Participants who undergo ECS were at significantly lower risk of intra-operative vomiting and nausea compared to their peers in the TCS group (Risk Ratio [RR] [95% CI] = 0.29 [0.10, 0.82]; I^2 =

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59.5%; p = 0.02) (Figure 10A). Post-operative visual analog scale (VAS) pain scores revealed that TCS patients experienced significantly higher pain levels compared to ECS (SMD [95% CI] = -2.01 [-2.30, -1.73]; I^2 = 98.6%; p = 0.00) (Figure 10B). To find the source of heterogeneity in the VAS analysis, meta-regression was performed with the ECS approach as the covariate. This approach may be one of the reasons for heterogeneity in a statistically significant manner (P=0.00).

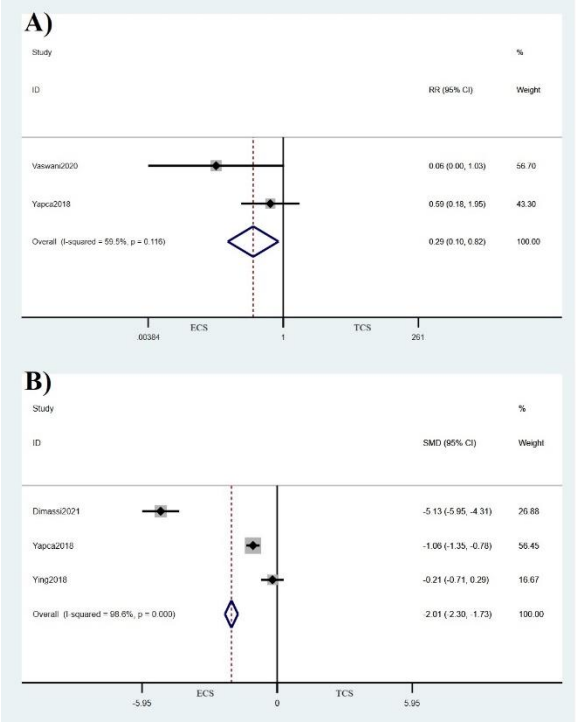

Figure 10. A) Forest plot for intra-operative vomiting and nausea of ECS vs. TCS B) Forest plot for post-operative VAS pain of ECS vs. TCS

In the sub-chronic complications' subset, the time until the first gas passage and the risk of urinary tract infection (UTI) were evaluated. Although the time until the first gas passage was significantly longer in TCS patients (SMD [95% CI] = -1.19 [-1.45, -0.92]; I^2 = 0; p = 0.00) (Figure 11A), ECS and TCS patients experience similar risk of urinary tract infection (UTI) (RR [95% CI] = 1.11 [0.47, 2.62]; I^2 = 0%; p = 0.82) (Figure 11B). Due to the importance of bladder injury in cesarean delivery, as reported by 3 studies in total, 1.5% of ECS (7/481) and none of TCS patients experienced bladder injury [4,22,23].

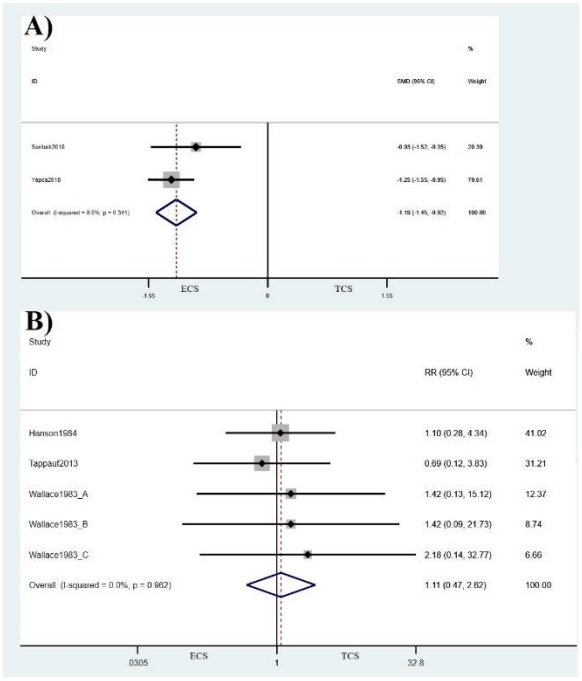

Figure 11. A) Forest plot for time until the first gas passage of ECS vs. TCS B) Forest plot for UTI of ECS vs. TCS

Neonatal Outcomes

We had sufficient data to analyze APGAR scores in ECS vs. TCS patients, The 1-minute (SMD [95% CI] = 0.00 [-0.13, 0.13]; I^2 = 0%; p = 1.00) and 5-minute APGAR (SMD [95% CI] = 0.05 [-0.08, 0.18]; I^2 = 0%; p = 0.48) was not different between cases and controls.

Discussion

The current systematic review and meta-analysis demonstrated the comparative efficacy of ECS versus TCS and within ECS techniques. Our findings illustrated no significant difference in total operation time between ECS and TCS, which challenges the traditional preference for TCS due to surgical efficiency. It should be noted that FAUCS as one of the ECS methods was associated with a longer operation time; however, classical paravesical ECS can be considered a faster alternative even compared to TCS. A critical concern for ECS is its increased blood loss in comparison with TCS. However, this increased blood loss did not translate into a considerable hemoglobin change after surgery.

The study further highlights that ECS patients are at a lower risk of intra-operative vomiting and nausea, which accounts for an important consideration for patient management and comfort during surgery. TCS patients reported higher levels of post-operative pain, pointing towards ECS as a potentially more comfortable postoperative experience for patients. The faster recovery of gastrointestinal function in ECS patients adds another dimension to the postoperative

[DOI: DOI: 1052547/sjrm.10.4.7]

benefits of this technique. Importantly, the risk of urinary tract infections, a common concern post-cesarean delivery, was found to be comparable between the two techniques, suggesting no additional risk with the choice of ECS.

As cesarean delivery is one of the most prevalent surgeries conducted globally, an ongoing effort is being made to identify a method that is attributed to the lowest rate of complications. Wylie et al. [33] concluded that opting for a low transverse incision is attributed to a generally better outcome. In other words, when compared to a classical incision, a low transverse incision results in reduced bleeding, facilitates easier repair, and leads to diminished adhesion formation. In addition, Olyaeemanesh et al. [34] compared the safety and effectiveness of the Misgav Ladach TCS technique and the transverse Pfannenstiel incision. Their meta-analysis showed that operation time, blood loss, and post-operative hospital stay in the Misgav Ladach TCS technique are significantly lower compared to transverse Pfannenstiel. Our findings highlighted the postoperative benefits of ECS, including quicker recovery of gastrointestinal function; however, the Misgav Ladach TCS technique showed less postoperative pain and faster wound healing. Although the reason why the Misgav Ladach TCS technique is correlated with fewer adverse outcomes was not discussed.

In ECS, the incision is made outside the peritoneal cavity, which avoids direct exposure to the abdominal organs. This might decrease the risk of contamination, reducing the likelihood of postoperative infections. TCS, which involves opening the peritoneal cavity, may theoretically have a higher risk of infection. It may also allow for better preservation of tissue planes as the lower uterine segment is incised, which leads to enhanced wound healing. It should be noted that, with the advent of antibiotics, ECS quickly lost popularity for a few decades. However, since the 1990s, antibiotic resistance has become a major global health issue [35]. According to estimates, bacterial antimicrobial resistance contributed to 4.95 million fatalities worldwide in 2019 and was directly responsible for 1.27 million deaths [36]. In this context, strategies that intrinsically reduce postoperative infection risk are increasingly important. ECS, by avoiding entry into the peritoneal cavity and minimizing exposure of intra-abdominal organs, theoretically lowers the chance of deep pelvic and abdominal infections. This advantage becomes particularly relevant in an era when prophylactic and therapeutic antibiotics may be less effective, underscoring ECS as a potentially valuable option in mitigating infection-related morbidity. Another important factor to consider is whether cesarean delivery is performed on a scheduled (elective) basis or under emergency circumstances [37]. Elective cesareans generally allow for better preparation, optimal surgical conditions, and reduced maternal stress, while emergency procedures are often associated with higher maternal and neonatal morbidity due to time constraints, increased blood loss, and higher infection risks [38]. The potential benefits of ECS, such as reduced postoperative pain and faster gastrointestinal recovery, may be most evident in scheduled procedures, where surgical precision can be maximized [39]. Conversely, in emergency scenarios, where rapid delivery is paramount, TCS may remain the more practical option due to quicker uterine access.

A crucial theoretical advantage of ECS is the lower disruption of physiological structures within the abdominal cavity. Based on our qualitative synthesis, we believe that ECS may be more applicable to particular groups of patients. For patients with previous abdominal surgeries who are at higher risk of adhesions, accessing the peritoneal cavity can be challenging. As ECS does not involve entering the abdomen, there may be a decreased risk of accidental injury to the intestines or other abdominal organs. For instance, in cases with a history of multiple cesarean deliveries, the ECS might be the preferred approach to avoid complications associated with adhesions and scar tissue. It should be noted that the surgeon's learning curve and accumulated cesarean experience is very important. Studies show that less experienced surgeons ("beginners") have significantly longer incision-to-delivery and incision-to-closure times, higher blood loss, and more postoperative complications compared to seasoned surgeons [40]. In one retrospective study of ten trainees, performance improvements (in operative time and incision-delivery interval) were most pronounced over the first 10-15 procedures, after which gains diminish [41]. Similarly, in a low-resource setting, associate clinicians performing cesareans reduced mean operative time substantially over their first 15 caesarean deliveries, and rates of surgical site infection were higher in that early phase [42]. These data suggest that comparing ECS versus TCS outcomes without accounting for operator experience may obscure true differences in risk and benefit. Especially, since our included studies contained a population of patients with previous cesarean deliveries and ECS was possible in those studies, we suggest that ECS, as a viable option, be considered before readily choosing TCS.

Strengths and limitations

The current study has several limitations. First, the heterogeneity among included studies can significantly impact outcomes, such as operation time and post-operative visual analog scale (VAS) pain scores. Although efforts, including sensitivity analysis, were made to explore the heterogeneity sources, some degree of unexplained heterogeneity remained. This heterogeneity can impact the reliability of the results. Second, our study provides a

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comprehensive overview of the available literature. As in the included papers, direct head-to-head comparisons between ECS and TCS were limited; therefore, we undertook additional well-designed comparative analysis to provide more conclusive evidence on the differences in surgical outcomes and complications between these approaches. Findings from this synthesis should be interpreted with caution. Third, a wide range of study designs, including randomized controlled trials (RCTs), retrospective cohort, observational, and case-control studies, were included. This variability in study designs may result in bias and can lead to limitations in terms of controlling for confounding variables. It potentially affects the validity of the qualitative synthesis results. Fourth, the variation in the risk of bias scores, which was assessed using established tools like the CONSORT and Newcastle-Ottawa Scale (NOS), may introduce bias into the results. Fifth, we do clearly believe that ECS should be done in selected cases. For example, it is likely that TCS is chosen for more complicated pregnancies, for those desiring tubal ligation or with potential placenta accrete. Also, there was no information regarding the risk of accidental peritoneal opening, the learning curve, and the lack of access to perform hemostatic procedures. Finally, it should be noted that several of the outcomes, such as blood loss, hemoglobin change, intra-operative nausea and vomiting, and postoperative gastrointestinal recovery were reported in only a small number of studies with relatively limited sample sizes. While these results provide valuable signals, the conclusions drawn from them must be interpreted with caution, as they may lack the robustness that comes with larger, multi-center trials.

Conclusions

In conclusion, the decision between ECS and TCS should be guided by various factors, including patient-specific factors, surgical team experience, and local healthcare practices. Our findings contribute to the existing body of knowledge and underscore the importance of further research to inform evidence-based clinical decision-making in cesarean deliveries. It is crucial to consider the limitations of the study when interpreting the results of the systematic review and meta-analysis, and further research, including larger and more standardized studies, is necessary to provide a more robust understanding of the clinical outcomes and complications associated with extraperitoneal cesarean delivery. Once again, keep in mind that ECS is not routinely used in practice or taught. We feel that with a well-designed education and practice, ECS may be a viable recourse in times of need.

Ethical Issue

This study was in accordance with the ethical issues for human subject research and confirmed by an ethical committee CRD42023422398 (09/05/2023) Informed consent was obtained from all subjects.

Conflict of Interests

There was no conflict of interest in this study.

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[DOI: DOI: 1052547/sjrm.10.4.7]