

Perioperative and Postoperative Complications During Total Laparoscopic Hysterectomy in Patients with a Previous Cesarean Section

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ABSTRACT **Background:** Cesarean section (CS) comprised almost one-third of all births. One of the complications after CS is intra-abdominal and pelvic adhesions formation. **Objectives:** To investigate whether a previous CS poses an additional perioperative or postoperative risk for complications when performing a total laparoscopic hysterectomy (TLH). **Methods:** We conducted a retrospective cohort study of women who had undergone a TLH between 2014 and 2020. Perioperative and postoperative complications were assessed according to the Clavien-Dindo classification system. Descriptive statistics were used to analyze the results. **Results:** In total, 190 women underwent TLH during the study period, 50 (26.5%) had a previous CS (study group) and 140 (73.5%) had no history of CS. The complication rates using the Clavien-Dindo classification system were similar in both groups; however, the major complications rate was not significantly higher in the study group (CS 6% vs. no CS 1.4%, $P = 0.08$). Urethral injury was the most common major complication (2, 4% vs. 1, 0.7%). The duration of surgery (125 min vs. 112 min, $P = 0.02$), estimated blood loss (174 ml vs. 115 ml, $P = 0.02$), and additional postoperative endoscopic interventions (4% vs. 0%, $P = 0.01$) and were significantly greater in patients with a previous CS. **Conclusions:** Although the need for postoperative endoscopic interventions, surgery duration, and estimated blood loss were significantly higher in patients with a previous CS, TLH remains a safe and recommended procedure for these patients. Major complications are rare and do not occur more frequently following a previous CS.

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Cesarean section (CS) is the most common major operation performed in the United States [1]. In 2017 CS comprised almost one-third of all births, totaling over 1.2 million procedures [2]. There is a constant rise in the prevalence of CS and by 2015 one in every five births was delivered by CS [3]. Several short- and long-term complications have been associated with CS [4,5].

One of the complications after CS is intra-abdominal and pelvic adhesions formation, which are reported to be present in up to 65% of patients after a single CS and increases with the number of CS performed [6]. These adhesions are related to an increased risk for bowel obstruction and chronic pain [5,7]. Adhesions can also pose difficulties in subsequent surgeries, which may result in an increased risk of complications such as inadvertent injury to abdominal organs, increased duration of surgery, and increased blood loss [8].

Total laparoscopic hysterectomy (TLH) is a minimally invasive approach for hysterectomies in which all the surgical dissections, ligations, and sutures are completed entirely laparoscopically, including the closure of the vagina [9]. Complications are the same as hysterectomy and laparoscopy combined and may include injury to adjacent structures (great vessels, ureter, bladder, and bowel) [10,11]. Postoperative complications may include vaginal cuff dehiscence, vesicovaginal fistula, infection, and hemorrhage [11].

The Clavien-Dindo classification system of surgical complications was introduced in 2004 and has gained popularity since. This classification system is based on ranking specific complications by the intervention used to manage them. Complications are defined as any deviation from the normal postoperative course. Each therapy given to the patient is categorized into one of 5 grades [Appendix 1, online version only]. This method of classification provides a uniform assessment of perioperative

and postoperative complications. The Clavien-Dindo classification system has been applied in various fields of surgery and has been previously used to assess complications following gynecological surgeries as well [12,13].

There is insufficient data regarding the impact of a previous CS on perioperative and postoperative complications following TLH. Findings from existing studies are somewhat conflicting. Wang et al. [14] found that the rate of inadvertent cystotomies varied between the previous CS and non-previous CS groups, 5% and 1.2% respectively. However, Lim et al. [15] stated that the number of prior CS had no effect on the rate of major complications. To the best of our knowledge, no previous studies have investigated this question using the Clavien-Dindo method of classification. The aim of this study was to investigate the impact of a prior CS on the risk of perioperative and postoperative complications following TLH using the Clavien-Dindo classification.

PATIENTS AND METHODS

This retrospective cohort study consisted of women who had undergone a TLH at a large university-affiliated tertiary referral center between the years 2014 and 2020. All the surgeries were performed by board certified gynecologic surgeons who were experienced laparoscopists. The study was approved by the institutional review board in accordance with Helsinki declaration. Inclusion criteria included women who had undergone a TLH for benign indications and age ≥ 18 years.

To isolate the effect of CS on the surgical outcomes of TLH, we excluded patients with a past medical history that might have caused abdominal or pelvic adhesions such as any abdominal/pelvic procedures other than CS, inflammatory bowel disease, endometriosis, or abdominal or gynecological malignancy. We defined the main exposure as having a previous CS and the control group as women without a history of CS.

Data were collected from computerized patient charts and included: background clinical and demographical characteristics such as age, ethnicity, gravidity, parity, body mass index (BMI), number of prior CS and indications for TLH; surgical characteristics including duration of surgery, estimated blood loss, major complications, and duration of hospitalization; postoperative treatment requiring pharmacological treatment, physiotherapy, blood transfusion, total parenteral nutrition, local anesthesia, general/epidural anesthesia, or admission to an intensive care unit (ICU).

Major complications were defined as bowel, ureter, bladder, great vessels injury, or vaginal cuff dehiscence. Any deviation from the standard postoperative treatment protocol within 6 weeks of surgery was graded according to the Clavien-Dindo classification system [Appendix 1, online version only].

Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 23 (SPSS, IBM Corp, Armonk, NY, USA). A P -value of < 0.05 was considered significant. In the current study, descriptive statistics were followed by a univariate analysis. Categorical variables were presented as percentages and compared using chi-square or Fisher's exact test as appropriate. Normally distributed continuous variables were presented as mean and standard deviation and compared using the Student's t test. Continuous variables that were not normally distributed were presented as median with an interquartile range and compared using the Mann-Whitney test. A multivariate logistic regression model analysis was conducted to examine whether previous CS was independently associated with perioperative and postoperative complications among women undergoing a TLH.

RESULTS

Between 2014 and 2020, 190 patients who had undergone a TLH for benign indications were included in our study. Among them, 50 patients (26.3%) had at least one previous CS (study group), and 140 patients (73.7%) had no history of CS (comparison group). Within the previous CS group, 34 patients (68%) had only one CS, eight (16%) had two CS, and another eight (16%) had three or more CS.

Baseline patient characteristics are presented in Table 1. Patients in the study group were slightly younger than the comparison group (47.5 vs. 51, $P = 0.01$) and had a higher rate of gravidity (5 vs. 4, $P < 0.01$). Most of the patients (71%) in the study population were of Jewish ethnicity. There was a higher rate of Bedouin Arab patients in the study compared to the comparison group (38% vs. 23.6%, $P = 0.04$).

Both groups had a mean BMI score above 25 and were considered overweight. The most frequent indication for TLH in both groups was menorrhagia (68%) followed by leiomyoma (49%).

Surgical outcomes are displayed in Table 2. Only five patients presented with major complications. All were detected postoperatively, except for one case of bowel injury that was diagnosed and treated during surgery. The

Table 1. Baseline characteristics: patients with and without a previous CS

			Previous CS (n=50)	No previous CS (n=140)	P-value
Age (mean ± SD)			47.52 ± 7.30	51.00 ± 8.36	0.01
BMI (mean ± SD)			30.45 ± 5.65	28.85 ± 6.03	0.10
Ethnicity n (%)	Jewish		31 (62.0%)	105 (75.0%)	0.04
	Bedouins		19 (38.0%)	33 (23.6%)	
	Other		0 (0.0%)	2 (1.4%)	
Gravidity	(mean, IQR)		5 (3–7.25)	4 (3–6)	< 0.01
Indication for TLH n (%)	Benign*	Total, n (%)	44 (88.0%)	120 (85.7%)	0.69
		Menorrhagia	38 (76%)	92 (65.7%)	0.81
		Leiomyoma	23 (46%)	71 (41.7%)	0.65
		Pelvic pain	4 (8%)	14 (10%)	0.71
		Other	1 (2%)	4 (2.8%)	0.76
	Pre-cancerous		6 (12.0%)	20 (14.3%)	0.69

*Numbers do not add up to total because some patients had more than one indication

BMI = body mass index, CS = cesarean section, IQR = interquartile range, SD = standard deviation, TLH = total laparoscopic hysterectomy

Bold signifies headlines

Table 2. Surgical outcomes: comparison between patients with and without a previous CS during and after performing TLH

			Previous CS (n=50)	No previous CS (n=140)	P-value
Duration of surgery (min, mean ± SD)			125.18 ± 35.43	112.70 ± 30.11	0.02
Estimated blood loss (ml, mean ± SD)			174.30 ± 263.84	115.21 ± 94.28	0.02
Major complications, n (%)			3 (6.0%)	2 (1.4%)	0.08
	Bowel injury, n (%)		0 (0%)	1 (0.7%)	0.91
	Ureter injury, n (%)		2 (4%)	1 (0.7%)	0.11
	Bladder injury, n (%)		1 (2%)	0 (0%)	0.56
Duration of hospitalization (days, median, IQR)			3 (3–3)	3 (3–3)	1.00
Readmission, n (%)			7 (14.0%)	13 (9.3%)	0.35

CS = cesarean section, IQR = interquartile range, SD = standard deviation, TLH = total laparoscopic hysterectomy

Bold signifies headlines

rate of major complications did not differ significantly between the groups (6% vs. 1.4% in the study and comparison groups, respectively) although a possible trend was noted ($P = 0.08$). Urethral injury was the most common major complication in our study and occurred twice in the previous CS group (4%) and once in the no CS group (0.7%). A bowel and a bladder injury each occurred only once.

The duration of surgery, measured from the first cut to the last stitch, was found to be significantly longer in the study group (125 min vs. 112 min, $P = 0.02$). Similarly, the estimated blood loss was significantly greater in the study group (174 ml vs. 115 ml, $P = 0.02$). How-

ever, no increased need for blood transfusions was noted in the study group. Nevertheless, neither the duration of hospitalization nor readmission rate were significantly different between the groups. No significant differences were found between the two groups in surgical complication gradings using the Clavien-Dindo Classification [Table 3]. However, patients in the study group had a non-significantly different higher rate of Grade III interventions (8% vs. 2.9%, $P = 0.12$), including surgical (6% vs. 2.1%, $P = 0.18$), radiological (2% vs. 0%, $P = 0.09$), and endoscopic (4% vs. 0%, $P = 0.01$) interventions. Although only the latter was found to be statistically significant, these results might suggest a trend.

Table 3. Clavien-Dindo grading and interventions: comparison of grades determined by Clavien-Dindo and the interventions included in that grade among patients with and without previous CS

Clavien-Dindo grade	Intervention*	Previous CS (n=50)	No previous CS (n=140)	P-value
Grade 0		35 (70%)	105 (75%)	0.49
Grade I		3 (6%)	7 (5%)	0.76
	Anti-emetics, n (%)	5 (10.0%)	10 (7.1%)	0.52
	Anti-pyretics, n (%)	1 (2.0%)	2 (1.4%)	0.78
	Analgesics, n (%)	1 (2.0%)	2 (1.4%)	0.78
Grade II		8 (16%)	23 (16.4%)	0.91
	Antibiotics, n (%)	12 (24.0%)	20 (14.3%)	0.12
	Blood transfusions, n (%)	2 (4.0%)	5 (3.6%)	0.89
Grade III		4 (8%)	4 (2.9%)	0.12
	Surgical intervention, n (%)	3 (6.0%)	3 (2.1%)	0.18
	Endoscopic intervention, n (%)	2 (4.0%)	0 (0.0%)	0.01
	Radiological intervention, n (%)	1 (2.0%)	0 (0.0%)	0.09
Grade IV		0 (0%)	1 (0.7)	0.91
	IC/ICU admission, n (%)	0 (0.0%)	1 (0.7%)	0.55
Grade V	Death of a patient, n (%)	0 (0.0%)	0 (0.0%)	NA
Grade (median, IQR)		0 (0–1.25)	0 (0–0.75)	0.44

*Numbers do not add up to total since some patients had more than one intervention

CS = cesarean section, IQR = interquartile range, SD = standard deviation, TLH = total laparoscopic hysterectomy

Bold signifies headlines

Table 4. Clavien-Dindo grades by number of previous CS: comparison of grades determined by Clavien-Dindo between groups divided by the number of previous CS

Grade	No Previous CS (n=140)	One CS (n=34)	Two CS (n=8)	Three or more (n=8)	P-value
Grade 0, n (%)	105 (75%)	23 (67%)	5 (62.5%)	7 (87.5%)	0.56
Grade I, n (%)	7 (5%)	2 (5.8%)	1 (12.5%)	0 (0%)	0.72
Grade II, n (%)	23 (16.4%)	5 (14.7%)	2 (25%)	1 (12.5%)	0.89
Grade III, n (%)	4 (2.9%)	4 (11.7%)	0 (0%)	0 (0%)	0.11
Grade IV, n (%)	1 (0.7%)	0 (0%)	0 (0%)	0 (0%)	0.95
Grade V, n (%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	NA

CS = cesarean section

The use of antibiotics for an infection was twofold more common in the study group (24% vs. 14.3%) but was not statistically significant ($P = 0.12$). One patient from the comparison group was admitted to the ICU directly from the operating room for observation after she developed pulmonary edema. She was stable and returned to the ward after several hours.

In the study group, the number of prior CS did not significantly affect the prevalence of periand postoperative interventions, as presented in Table 4. Consequently, even when comparing women with multiple previous CS

to women with no previous CS, there was no significant difference in the Clavien-Dindo classification grading.

DISCUSSION

The aim of this study was to examine whether a previous CS increases the risk of perioperative and postoperative complications after a TLH. We found no significant differences regarding perioperative and postoperative complications between patients with or without a previous CS. Although not statistically significant, there might be

a trend toward a higher rate of major complications (6% vs. 1.4% study and comparison groups, respectively; $P = 0.08$). Moreover, we noted that patients with a previous CS lost more blood ($P = 0.02$) during surgery and the duration of the surgery was longer ($P = 0.02$). In addition, Grade III interventions were close to threefold more common in the study group (8% vs. CS 2.9%), but this was not statistically significant ($P = 0.12$).

Because the rate of CS is increasing globally [3], it is important to assess the associated complications, and specifically long-term complications. We investigated the risks associated with TLH in patients with a previous CS. Both CS and TLH are relatively safe procedures and major complications are rare, but it is important to be aware of any possible long-term consequences. We found no significant increase in major complications during TLH in patients with a prior CS, like the results of Lim et al. [15].

In a study by Wang et al. [14], of 574 patients who underwent a TLH, 141 had a prior CS. Their findings showed a significantly increased rate of inadvertent cystotomies in the prior CS group (5% vs. 1.2%, $P = 0.012$) and a very high rate of major complications (14.2% vs. 8.8%). These rates of major complications are much higher than in our study. In contrast to our study, they included hemorrhage as a major complication; the rate was approximately 7% for each group. This finding may explain the different rates that were noted in our study. In our study, we expected a gradual increase of major complications as the number of previous CS increased, as described by Lindquist et al. [16]. Their study included a large population of 7685 women and showed that the risk for complications after hysterectomy increased with the number of previous CS. However, we did not find a significant association between complications and the number of previous CS. It is possible that the small number of patients with multiple CS in our study was underpowered to find a significant difference. Another possible difference between our findings and those of Lindquist et al. may be the fact that they did not calculate the complication risk solely for TLH but included vaginal and abdominal hysterectomies as well, which might have different complication rates.

In our study, a significant increase in the duration of TLH was noted in patients with prior CS. In a study of 482 patients, in which 158 of them had a prior CS [15], Lim et al. found that TLH took 7 minutes longer in patients with a prior CS. Likewise, we found a significant increase of 13 minutes in the study group. The increased duration of surgery could be attributed to adhesions formed following CS, which may change the normal anatomy and surgical planes. We were able to demonstrate a significantly high-

er estimated blood loss during the surgery, which, to the best of our knowledge, other published studies have not addressed. This result can be also explained by adhesion formation and longer surgery duration. Saban and colleagues [17] demonstrated that adhesions attributable to a previous CS increase the risk for hemorrhagic complications in a subsequent CS. The possible clinical significance of longer duration of surgery and blood loss is a greater burden on the operating room and longer hospitalization duration, leading to a greater financial burden on the healthcare system.

In our study, patients with previous CS were significantly younger at the time of TLH, which is consistent with other published studies [15,18,19]. There was a significantly higher rate of Bedouin Arab patients in the study group. Bedouin Arab women are known to give birth at a younger age and have a higher gravidity than the general population. After adjusting for age and gravidity, the results remained unchanged.

Our study has several strengths. It was conducted at a large tertiary teaching medical center that serves a population of over 700,000 people. This population is heterogeneous and diverse and therefore increases the generalizability of our results.

We used the Clavien-Dindo classification of surgical complications in our study to give a uniform and validated assessment of complications.

The data for this study were collected from multiple sources, including patient electronic medical records, surgery reports, and a nationwide medical information sharing system. All these sources, used together, provide greater validity and reliability to the collected data, thus decreasing the risk of missing data that may be a problem in retrospective studies.

There are some limitations in our study. The retrospective design prevented us from acquiring specific types of data that would have enabled us to accurately record a prospective model, such as the time interval between the last CS and the TLH. Our population sample size may have possibly been too small to achieve a significant difference between the groups using the Clavien-Dindo classification.

CONCLUSIONS

We did not find a significantly increased risk of major complications associated with TLH in patients with a previous CS, although a trend was noted. Patients undergoing TLH with a prior CS could be reassured that major complications of TLH are rare. Additional studies are required, preferably multi-centered studies, to further determine the risk of previous CS on TLH complications.

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Just as appetite comes by eating so work brings inspiration.

Igor Stravinsky (1882–1971), Russian composer

Capsule

Mitochondrial DNA oxidation propagates autoimmunity by enabling plasmacytoid dendritic cells to induce TFH differentiation

Stress-induced oxidized mitochondrial DNA (Ox-mtDNA) fragments enter the cytoplasm, activating the NLRP3 inflammasome and caspase-1 and enabling gasdermin-D-mediated circulatory release of mtDNA. Elevated amounts of circulating mtDNA, presumably oxidized, have been detected in older individuals and patients with metabolic or autoimmune disorders. Xian et al. showed that sustained Ox-mtDNA release, triggered by a prototypical NLRP3 inflammasome activator, induces autoantibody production and glomerulonephritis in mice. Similar autoimmune responses, dependent on plasmacytoid dendritic cells (pDCs) and follicular helper T (TFH) cells, are elicited by in

vitro-generated Ox-mtDNA, but not by non-oxidized mtDNA. Although both mtDNA forms are internalized by pDCs and induce interferon- α , only Ox-mtDNA stimulates autocrine interleukin (IL)-1 β signaling that induces co-stimulatory molecules and IL-21, which enable mouse and human pDCs to induce functional TFH differentiation, supportive of autoantibody production. These findings underscore the role of pDC-generated IL-1 β in autoantibody production and highlight Ox-mtDNA as an important autoimmune trigger, suggesting potential therapeutic opportunities.

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