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The anesthetic approach to repeated cesarean sections: A prospective cohort study

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ABSTRACT

Objective: Each repeat cesarean section (CS) potentially adds surgical complexity. The determination of appropriate anesthesia strategy to meet the surgical challenge is of crucial importance for the maternal and neonatal outcome.

Study design: This prospective cohort study was conducted from 1-Jan-2021 to 31-Dec-2021 at a single large obstetric centre of all repeat CS. We compared the characteristics and the appropriateness of the anesthesia techniques for low-order repeat CS (LOR-CS) (1 or 2 previous CS) and high order repat CS (HOR-CS) group (3 or more repeat CS).

Results: During the study period, 1057 parturients met the study entry criteria, with 821 parturients in the LOR-CS group and 236 parturients in the HOR-CS group. The use of spinal anesthesia was more common for HOR-CS 84.3%. Overall surgical time varied between LOR-CS (38 min, 29–49) and HOR-CS (42 min, 31–57) ($p = 0.004$). The rate of moderate and severe adhesions was relatively high in HOR-CS and the duration of overall surgical time for cases with mild adhesions was 38 min (29–48), for moderate adhesions was 44 min (34.8–56.5), and for severe adhesions was 56 min (44.8–74.3). There was no significant difference in the Estimated Blood Loss (EBL) between LOR-CS and HOR-CS, with values of 653 ± 292 ml vs. 660 ± 285 ml, respectively.

Conclusion: Our data indicate that spinal anesthesia, standard monitoring and regular anesthetic setup are safe and suitable for the majority of HOR-CS, except in cases with high suspicion of placental accreta spectrum.

1. Introduction

Cesarean section (CS) is one of the most common surgical procedures worldwide. The frequency of CS is on the rise each year, and concurrently, the rate of repeated CS is also increasing [1–4]. A previous CS is the main reason necessitating subsequent surgical deliveries ↱[5]. In some countries CS rate reaches more than 50%, notably in the Dominican Republic (58.1%), Brazil (55.7%), Cyprus (55.3%), Egypt (51.8%), and Turkey (50.8%), which also represented the highest CS rate in South America, Asia, and Africa. In Europe, the highest CS rate is reported in Romania (46.9%) [6].

National guidelines from various countries, including ACOG [7], RCOG [8], COGS [9], generally do not specifically address management issues related to repeat CS, particularly in the HOR-CS group (four or more CS). Each repeat CS may be more complex than the preceding one, and there is an elevated risk of abnormal placentation (accreta, increta,

Abbreviations: BTL, Bilateral Tubal Ligation; IOC, Intraoperative Complications; OB, Obstetric; HOR-CS, high order repat CS; LOR-CS, low-order repeat CS; PAS, placenta spectrum; REBOA, Resuscitative Endovascular Balloon Occlusion of the Aorta.

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and percreta). This risk can lead to more severe maternal morbidity or even mortality [10].

Given the global trend toward an increase in the number of CS, it is crucial to comprehend the surgical characteristics and complications that may arise in women with HOR-CS and to determine appropriate anesthesia strategies.

2. Methods

This prospective cohort study was conducted during a period of one year from 1-Jan-2021 to 31-Dec-2021 in Shaare Zedek Medical Center (Jerusalem, Israel). The study was conducted according to the observational study protocol - STROBE.

2.1. Study population

The study protocol received approval from the Institutional Review Board (IRB) in Jerusalem, Israel, with the IRB number SZMC-0415–20. In consideration of the nature of the study, a waiver of informed consent was granted. All consecutive women undergoing repeat CS at the Shaare Zedek Medical Center were included in the study. This inclusion criterion was established to ensure the comprehensive collection of data from the entire population, thus establishing the denominator and mitigating selection bias. No exclusion or dropout criteria were applied. For the purpose of this study, "LOR-CS" was defined as a group of parturients with a medical history of 1 or 2 previous CS, while "HOR-CS" was defined as a group of parturients with a medical history of 3 or more repeat CS. No distinction was made between planned, urgent and emergency cases. It is important to explicitly note that primary CS were excluded from the study, or the numbers did not align accordingly.

2.2. Clinical setting

Tertiary care obstetric service, with 15,983 deliveries and an 13.65% CS rate during the study period (2021).

2.3. Study protocol

All cases were retrieved from the medical center's electronic database "AZMA". All women that delivered by CS and had with prior one or more CS were included in the study.

Spinal anesthesia, epidural anesthesia, and combined spinal-epidural anesthesia (CSE) were administered. The standard protocol for spinal anesthesia established at the center include heavy bupivacaine 10 mg with intrathecal morphine 150 mcg and fentanyl 10–15 mcg.

Intra-operative adhesions are reported in electronic records and were defined as adhesions perceived by the surgeon as mild, moderate, severe.

Obesity was defined as BMI index $\geq$ 30 kg/m^2.

Estimated blood loss was defined by surgeon accordion to the visual method.

Blood product therapy was mainly carried by clinical situation or due to results of Thromboelastography.

Organ injury (bowel and bladder) was detected intraoperatively.

2.4. Primary outcome measures

The rates of prolonged surgery, defined as surgery time exceeding 60 and 90 min from skin incision to skin closure, and the type of anesthesia, blood loss during CS. Additionally, the rate of conversion to general anesthesia for reasons other than failed regional anesthesia.

2.5. Secondary outcome measures

The rates and severity of intra-operative adhesions, abnormal placentation (placenta previa, invasive placenta spectrum (PAS)), fetal outcomes (e.g., Apgar scores, mortality) and maternal outcomes such as the rate of peripartum hysterectomy, blood product transfusions, utilization of additional intraoperative monitoring, use of Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) technique, use of Cell-Saver technique, ICU admissions and length or hospitalization.

2.6. Data collection, management and statistical analysis

The data were collected independently by two researchers (RM and TA). Subsequently, the data were cross-checked by a third researcher (JW).

Data were analyzed using IBM SPSS Statistics 25 for Windows (SPSS, Chicago, IL) and Microsoft Office Excel 2013, for Relative risk (RR, 95% CI, NNT) data was processed using MedCalc 20 for Windows (MedCalc Software Ltd, Belgium). The level of significance was considered to be 95% ($p \leq 0.05$).

Conformity of the data to normal distribution was assessed using the Kolmogorov-Smirnov test. If the data did not have a statistically significant deviation of the sample distribution from the normal level of the probability distribution, the mean (M) and standard deviation ($\pm$sd) were used to represent the data. If the study data had a statistically significant deviation of the sample distribution from the normal level of the probability distribution, medians (Me) and interquartile ranges (Q1-Q3) were used to present the data. To compare the groups, statistical hypotheses were formulated about the difference between the samples in general, which were tested using the parametric Student's t test and the nonparametric U-Mann-Whitney test in the case of two compared groups. Relative risk (RR, 95% CI) was determined to assess the difference in events between the LOR-CS and HOR-CS groups.

3. Results

3.1. Common outcome measures

During the study period 1057 women met the study entry criteria, group LOR-CS – 821 (77.7%) parturients and HOR-CS – 236 (22.3%) parturients (Fig. 1).

Parturient in the HOR-HS group were characterized by higher gravidity (6 vs 4) and parity (4 vs 2), than group LOR-CS (Table 1). History from previous surgical report or finding at repeat surgery of severe adhesions were more likely for parturients with HOR-CS RR 7.54 (95% CI 3.86–14.71).

Obesity was more likely in the HOR-CS group, the risk of CS Category I [11] was less likely in the HOR-CS group (RR 0.35, 95% CI 0.23–0.54), whereas the risk for CS Category IV was more likely in the HOR-CS group (RR 1.49, 95% CI 1.33–1.68) (Table 2). Planned CS was more common in the HOR-CS group, RR 1.55 (95% CI 1.42–1.70).

3.2. Anesthesia outcome measures

Most CS in both groups were performed under neuraxial anesthesia,

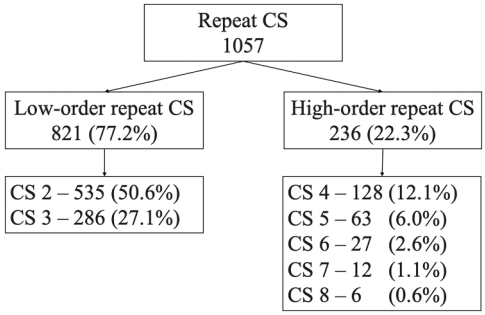

Fig. 1. Number of repeat caesarean sections.

Table 1
Demographic and pregnancy characteristics.

	LOR-CS (n = 821) Median (IQR)	HOR-CS (n = 236) Median (IQR)
Maternal age (years)	33 (29–36)	35 (32–38)
BMI (kg/m^2)	29 (27–33)	31 (28–35)
Gestational age at delivery (weeks)	38 (37–39)	37 (36–38)
Gravidity	4 (3–6)	6 (5–8)
Parity	2 (1–4)	4 (3–5)
	LOR-CS n (%)	**HOR-CS n (%)**
Previous emergency CS	346 (57.9%)	93 (39.4%)
History of severe adhesions	12 (1.5%)	26 (11.0%)
Previous uterine surgery	86 (10.5%)	23 (9.7%)
Previous abdominal surgery	45 (5.5%)	26 (11.0%)
Uterine abnormalities	18 (2.2%)	7 (3.0%)
IVF achieved pregnancy	40 (4.9%)	5 (2.1%)
Multiple Pregnancy	26 (3.2%)	5 (2.1%)

CI - confidence interval; IQR - Interquartile range; IVF - In vitro fertilization

Table 2
Medical and obstetric characteristic.

	LOR-CS (n = 821), n (%)	HOR-CS (n = 236), n (%)	Relative Risk (95% CI)
Medical history			
Obesity (BMI ≥ 30 kg/m^2)	270 (32.9%)	113 (47.9%)	1.19 (1.03–1.38)
Preoperative pregnancy complications			
Gestational diabetes mellitus	81 (9.9%)	29 (12.3%)	1.24 (0.84–1.86)
Abnormal placentation	21 (2.6%)	11 (4.7%)	1.82 (0.89–3.73)
Preeclampsia	25 (3.0%)	6 (2.5%)	0.84 (0.35–2.01)
Gestational thrombocytopenia	18 (2.2%)	7 (3.0%)	1.35 (0.57–3.20)
CS Emergency Scale			
1	198 (24.1%)	20 (8.5%)	0.35 (0.23–0.54)
2	77 (9.4%)	16 (6.8%)	0.73 (0.43–1.21)
3	178 (21.7%)	42 (17.8%)	0.82 (0.60–1.11)
4	368 (44.8%)	158 (66.9%)	1.49 (1.33–1.68)
Indication for CS			
Previous CS	517 (63.0%)	220 (93.2%)	1.48 (1.39–1.58)
Fetal distress	168 (20.5%)	9 (3.8%)	0.19 (0.10–0.36)
Abnormal placentation	21 (2.6%)	11 (4.7%)	1.82 (0.89–3.73)
Preeclampsia	13 (1.6%)	3 (1.2%)	0.80 (0.23–2.79)

CI - confidence interval; BMI – Body Mass Index

with spinal anesthesia being the most common technique (Table 3). The use of spinal anesthesia was more likely for HOR-CS, RR 1.13 (95% CI 1.07–1.20), compared to the epidural technique, RR 0.04 (95% CI 0.01–0.25). The rate of CSE was significantly higher in the HOR-CS group, RR 3.33 (95% CI 1.89–5.86).

General anesthesia (GA) was used as the primary anesthesia in 51 cases (4.8%) across both groups, with no significant difference in GA rates between LOR-CS and HOR-CS (Table 3). Seven patients in the LOR-CS group required a conversion to GA from regional anesthesia due to intraoperative complications. Five additional patients (four in the LOR-CS group and one in the HOR-CS group) received GA due to failure of regional anesthesia.

Table 3
Anesthesia for cesarean section.

	LOR-CS (n = 821), n (%)	HOR-CS (n = 236), n (%)	Relative Risk (95% CI)
Spinal	651 (79.3%)	199 (84.3%)	1.13 (1.07–1.20)
Epidural	98 (11.9%)	1 (0.4%)	0.04 (0.01–0.25)
CSE	23 (2.8%)	22 (9.3%)	3.33 (1.89–5.86)
GA	38 (4.6%)	13 (5.5%)	1.20 (0.65–3.20)
Anaesthesiologist level			
Resident	234 (28.5%)	58 (24.6%)	0.86 (0.67–1.10)
Fellow	82 (10.0%)	29 (12.3%)	1.23 (0.83–1.83)
Attending	505 (61.5%)	149 (63.1%)	1.03 (0.92–1.15)

GA - General Anesthesia; CSE - Combined Spinal-Epidural; RA – Regional Anesthesia; IOC – Intraoperative Complications

3.3. Surgical and maternal outcomes

The time from skin incision to delivery did not show a significant difference between the groups, being 7 min (4–10) vs. 7 min (5–11) (p = 0.51). However, the overall surgical time differed between LOR-CS (38 min, 29–49) and HOR-CS (42 min, 31–57) (p = 0.004). The number of cases with overall surgical time exceeding 60 min was 107 (13%) for LOR-CS and 51 (21.6%) for HOR-CS, resulting in a RR of 1.66 (95% CI 1.23–2.24). For cases with surgical time exceeding 90 min, the numbers were 25 (3.1%) for LOR-CS and 10 (4.24%) for HOR-CS, with a RR of 1.39 (95% CI 0.68–2.86).

The overall rate of moderate and severe adhesions was 2.62 (95% CI 2.12–3.25), with a number needed to treat (NNT) of 3.77 (95% CI 3.10–4.84). The rate of peripartum hysterectomy was higher in the HOR-CS group (Table 4).

The length of overall surgical time for cases with fourth CS was 41 min (30–54.5), for fifth CS was 44 min (32–55), for CS sixth was 43 min (30–55), for CS seventh was 42.5 min (26.3–64.5), and for CS eighth was 41 min (31.3–67.3). There was no significant difference between CS from 4 to 8 (Kruskal–Wallis H test p = 0.865).

The length of overall surgical time for all cases with mild adhesions was 38 min (29–48), for moderate adhesions was 44 min (34.8–56.5), and for severe adhesions was 56 min (44.8–74.3). There were significant differences between mild, moderate, and severe adhesions (Kruskal–Wallis H test p < 0.0001).

One case of admission to the intensive care unit (ICU) in the HOR-CS group was a patient with pulmonary embolism (PE). In the LOR-CS group, there were four cases: PE, HELLP syndrome, postpartum hemorrhage (PPH) and coagulopathy necessitating a relaparotomy due to

Table 4
Operative complications and additional surgical procedures.

	LOR-CS (n = 821), n (%)	HOR-CS (n = 236), n (%)	Relative Risk (95% CI)
Degree of adhesions			
Mild	208 (25.3%)	55 (23.3%)	0.92 (0.70–1.19)
Moderate	66 (8.0%)	52 (22.0%)	2.74 (1.96–3.83)
Severe	68 (8.3)	46 (19.5%)	2.35 (1.66–3.32)
Urinary bladder injury and repair	8 (1.0%)	4 (1.7%)	1.74 (0.53–5.73)
Bowel injury and repair	3 (0.4%)	2 (0.8%)	-
BTL	32 (3.9%)	20 (8.5%)	2.17 (1.27–3.73)
Hysterectomy	1 (0.1%)	4 (1.7%)	13.92 (1.56–123.91)
Relaparotomy for bleeding control	2 (0.2%)	2 (0.8%)	-
ICU admission	4 (0.5%)	1 (0.4%)	-

BTL- Bilateral Tubal Ligation

urinary bladder injury.

There was no significant difference in Estimated Blood Loss (EBL) between LOR-CS and HOR-CS, with values of 653 ± 292 ml vs. 660 ± 285 ml, respectively. Furthermore, the rate of PPH (EBL ≥ 1000 ml) was similar, with a RR of 1.19 (95% CI 0.85–1.67).

The volume of infusion therapy administered was 823 ± 392 ml for LOR-CS and 953 ± 573 ml for HOR-CS, resulting in a mean difference of 121 ml (95% CI 57–185), with a p-value of < 0.001. There was no difference in blood product between LOR-CS and HOR-CS groups, such as red packed cells (9 (1.1%) vs 2 (0.8%)), fresh frozen plasma (4 (0.5%) vs 1 (0.4%)) and platelets (2 (0.2%) vs 1 (0.4%)). Other manipulations (invasive blood pressure, central venous pressure, Cell Saver, REBOA) between the two groups were similar.

The number of days to discharge differed, being 5.5 ± 1.6 days for LOR-CS and 5.9 ± 2.4 days for HOR-CS (p = 0.002).

3.4. Neonatal outcomes

Apgar scores at 1 min and 5 min were similar in both groups. However, the need for Continuous Positive Airway Pressure (CPAP) or Mechanical Ventilation was more common in the HOR-CS group, with a RR of 2.17 (95% CI 1.16–4.08). Other neonatal outcomes exhibited no significant differences between the two groups (Table 5).

4. Discussion

The current study presents data from a large cohort of repeat CS deliveries with special focus on the anesthetic aspects of perioperative management for repeat CS. Reevaluation of a previous similar study conducted in 2010 in our center, showed that the total number of HOR-CS cases at our center increased by 3.3% annually - from 129 (7.5%) to 236 (10.8%) over an 11-year period [12].

The data obtained in this study align with the findings from a prospective cohort study conducted at our center [12]. The presence of adhesions in the medical history of the HOR-CS group was also affirmed by a higher incidence of intraoperative adhesions, both moderate and severe. Additionally, surgical time exceeded one hour more frequently in the HOR-CS group, similar to observations made 11 years ago at our center. The incidence of PAS was comparable between the LOR-CS and HOR-CS groups. The total number of placental abnormalities increased over the 11-year period, due to increased cases of placenta previa, against the backdrop of a single cases of placenta accreta in the HOR-CS groups.

During the study, 12 (1.13%) cases of bladder injury were identified, slightly higher than the general statistics. A study by L. Salman et al. [13] reported a 1.03% incidence of bladder injury with repeated CS, while Khalil AS et al. [14] found a frequency of 0.5% for HOR-CS.

Although the absolute rate of hysterectomies in our study in the HOR-CS group decreased from the 11-year-old study, the total number per 1000 births decreased from 23 per 1000 births (2.3%) to 17 per 1000 births (1.7%) in patients with HOR-CS, as a result of the use of REBOA [15]. In our analysis, only one patient from the HOR-CS group was admitted to the ICU with PE and we associate this with the use of REBOA [15].

Table 5
Neonatal outcomes.

	LOR-CS (n = 821), n (%)	HOR-CS (n = 236), n (%)	Relative Risk (95% CI)
Need for oxygen	55 (6.7%)	20 (8.5%)	1.26 (0.77–2.07)
Need for ventilation	40 (4.9%)	18 (7.6%)	1.56 (0.91–2.68)
Need for CPR	6 (0.7%)	0 (0%)	-
Need for NICU	69 (8.4%)	22 (9.3%)	1.11 (0.70–1.75)
Need for CPAP or MV	24 (2.9%)	15 (6.4%)	2.17 (1.16–4.08)

CPAP - Continuous Positive Airway Pressure; CPR - Cardiopulmonary Resuscitation; MV - Mechanical Ventilation; NICU - Neonatal Intensive Care Unit

Patients with HOR-CS are more likely to undergo elective surgery compared to LOR-CS patients, who tend to have indications for CS falling under Category I urgency. This is due to a higher frequency of Trial of Labor After CS (TOLAC) in LOR-CS, resulting in indications for CS such as fetal distress, arrest of labor, and maternal request. These factors influence the choice of anesthesia in laboring patients with epidural analgesia, leading to a higher incidence of epidural anesthesia in the LOR-CS group.

Spinal anesthesia, as well as CSE anesthesia, is more frequently performed in the HOR-CS group. CSE anesthesia is particularly chosen due to the potential extension of surgery and the need to prolong anesthesia for more than 90 min, although there are no more such cases in the HOR-CS group than in the LOR-CS group (10 (4.24%) versus 25 (3.1%), respectively). The percentage of GA in the HOR-CS group remained consistent as 11 years earlier (5.5% vs. 5.4%). Conducting randomized controlled trials for this research question presents significant challenges. Spinal anesthesia is the preferred method for CS due to its lower risk of anesthetic complications compared to GA. Women should be informed about the choice of anesthesia method, and their consent should be obtained during discussions regarding anesthesia.

In recent years, a relatively new method for limitation of blood loss during surgery, REBOA, has been utilized. Initially used in trauma management, REBOA is now being employed for obstetric patients with massive bleeding or for the prevention of bleeding in patients with suspected Placenta Accreta Spectrum (PAS) [16]. Perioperative blood loss with REBOA does not exceed 1 liter, and the rate of cesarean hysterectomy is lower than 20% [15,17,18]. In our study the rate of peripartum hysterectomy was higher in the HOR-CS group, but less then an 11-year period [12].

Our data did not reveal a significant risk of intraoperative surgical complications between groups, which is not consistent with the results of previously published studies [19–21].

Given the high risk of developing PPH in HOR-CS with abnormal placentation, the REBOA technique was more frequently employed, often in conjunction with Cell Saver.

Neonatal outcomes did not show significant differences between the groups, except for a higher need for CPAP therapy and invasive ventilation in HOR-CS, possibly due to the median gestational age being 37 weeks in this group.

The limitations of this study include that the analysis of surgical time did not include an assessment of the obstetrician's experience (resident, fellow, attending). However, the standard practice at our center mandates the involvement of an attending obstetrician during CS, irrespective of whether it's a LOR-CS or HOR-CS. In our study we did not evaluate presence of endometriosis in surgical field or patients history.

5. Conclusion

We have observed a significant increase in frequency of LOR-CS and HOR-CS. The most significant finding of this study is that, despite the higher incidence and severity of adhesions in HOR-CS, spinal anesthesia has proven to be sufficient for the majority of HOR-CS cases. The rate of conversion to GA did not differ significantly compared to that of low LOR-CS. Moreover, our results suggest that preparation for HOR-CS does not need to deviate from routine practices in terms of epidural catheter placement, monitoring, and anesthesia staff, except in cases where PAS is highly suspected.

This strategy necessitates the engagement of a skilled interdisciplinary team, effective pre- and intraoperative communication, and adaptability for the best possible case management.

CRediT authorship contribution statement

Rasha Mehelvus: Data curation. **Alexander Ronenson:** Writing – original draft, Formal analysis. **Stephen H Halpern:** Writing – review & editing. **Sorina Grisaru-Granovsky:** Writing – review & editing. **Jacob**

Weinstein: Data curation. **Tamer Akawi:** Data curation. **Yaacov Gozal:** Supervision. **Daniel Shatalin:** Writing – review & editing. **Alexander Ioscovich:** Writing – review & editing, Supervision, Conceptualization.

Declaration of Competing Interest

None.

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