INTRODUCTION

The timing of delivery has been a matter of great concern in the recent decade, and the literature is based largely on cohort studies. Trying to balance maternal and perinatal risks, several prospective studies have examined the outcomes of elective induction of labor (IOL) at 39 weeks versus expectant management. The ARRIVE trial in 2018 concluded that IOL at 39 weeks in low-risk nulliparous women resulted in significantly lower rates of cesarean section (CS), with no effect on perinatal adverse outcomes. It was followed by another randomized controlled trial concluding that IOL at 39 weeks had no effect on CS rate or adverse maternal and neonatal outcomes, as compared to expectant management.

As repeat elective CS is associated with inherent maternal risks, and for the purpose of decreasing CS rates, women with a previous CS are encouraged to undergo a trial of labor after cesarean section (LAC) when clinically appropriate. However, LAC is associated with several...
adverse maternal outcomes including, among others, the risk of uterine rupture, ranging 0.3–0.7%. Therefore, IOL in LAC may pose a true clinical dilemma. Generally, IOL among women undergoing LAC is performed for medical indications. However, considering the results of the ARRIVE trial, it is interesting to study whether the same effects observed following IOL at 39 weeks are present among women undergoing LAC when compared to expectant management. Currently, literature regarding this topic is lacking.

The purpose of this study is to compare LAC outcomes of women with no prior vaginal delivery that are undergoing IOL at 39\(\frac{0}{7}\) to 39\(\frac{6}{7}\) weeks of gestation with LACs occurring at ≥40\(\frac{0}{7}\).

## METHODS

### 2.1 Patients

This is a retrospective cohort study. The study cohort consisted of women undergoing a LAC with no prior vaginal delivery. All deliveries occurred at one tertiary medical center, from March 2011 to March 2020. We included women with a live singleton fetus in vertex presentation, with one prior low transverse uterine incision. We excluded women with more than one prior CS. We allocated the study cohort into two groups: IOL at 39\(\frac{0}{7}\) to 39\(\frac{6}{7}\) and all LACs occurring at ≥40\(\frac{0}{7}\). A further analysis compared IOL at 39\(\frac{0}{7}\) to 39\(\frac{6}{7}\) to IOL at ≥40\(\frac{0}{7}\) weeks of gestation.

Methods for IOL included oxytocin administration, extraamniotic balloon and amniotomy. Oxytocin is administrated at a rate of 1 milliunit per minute, with gradual increase of 1–1.25 milliunits per minute every 30 minutes to a maximal rate of 15 milliunits per minute. Extraamniotic balloon insertion is performed as follows: we administer a 22F Foley catheter through the cervix under direct visualization with the use of a sterile vaginal speculum. Before insertion, the cervix is cleansed with aseptic solution. Once the catheter passes the internal os, the balloon is inflated with 40–60 mL 0.9% NaCl solution, and the external end of the catheter is taped to the inner part of one of the thighs.

The primary outcome of the study was a composite of adverse neonatal outcomes including any of the following: Apgar scores <5 at 1 minute and <7 at 5 minutes, umbilical cord arterial pH <7, umbilical cord arterial base excess ≥12 mEq, neonatal intensive care unit (NICU) admission, mechanical ventilation use, hypoxic ischemic encephalopathy, and hospital length of stay >6 days after delivery. Secondary outcomes included a composite of adverse maternal outcomes including uterine rupture, postpartum hemorrhage, and length of stay >4 days after delivery. An additional secondary outcome was the mode of delivery.

### 2.2 Data collection

We collected the following variables from the electronic health record: maternal characteristics including maternal age, immigration and smoking status, body mass index (BMI) at admission to delivery unit, height and gestational weight gain, diabetic and hypertensive disorders; prior CS characteristics including gestational age at delivery, indications for the prior CS, cervical dilation and labor stage at prior CS, and birthweight at prior CS; current delivery characteristics including gestational age at delivery, sonographic estimated fetal weight, inter-delivery interval from prior CS, oxytocin administration, epidural analgesia, presence of meconium-stained amniotic fluid and intrapartum fever; mode of delivery and indication for unplanned CS; maternal outcomes including uterine rupture, postpartum hemorrhage, length of stay after delivery; neonatal characteristics and outcomes including birthweight, birthweight percentile, Apgar scores at 1 and 5 minutes, arterial pH and base excess, NICU admission, need for mechanical ventilation, hypoxic ischemic encephalopathy and length of stay after delivery.

We defined hypertensive disorders of pregnancy according to the American College of Obstetricians and Gynecologists (ACOG), integrating gestational hypertension and preeclampsia. Diabetic disorders were defined as either pregestational diabetes, in accordance with the American Diabetes Association criteria, or gestational diabetes mellitus, based on the diagnostic thresholds established by Carpenter and Coustan. We defined intrapartum fever as temperature of at least 38.0° Celsius that persists when the temperature is repeated after 30 minutes or a single oral temperature of 39°C (102.2 F). Birthweight percentiles were calculated using local, population-based live-born infants’ birth weight curves.

### 2.3 Statistical analysis

We performed univariable analysis using Chi square test and Fisher’s exact test as appropriate. We used the student t-test for analysis of continuous variables with normal distribution and the Mann–Whitney U test for analysis of continuous variables with skewed distribution. Multivariable logistic regression analysis was used to adjust for potential confounding factors for adverse maternal outcomes including IOL, maternal age, BMI, presence of diabetic or hypertensive disorders. Factors were reported as odds ratio (OR) and 95% confidence interval (CI). Potentially associated factors included those identified by univariable analysis (P <0.05). A two-sided P <0.05 indicated statistical significance. The data were analyzed using Software Package for Statistics and Simulation (IBM SPSS version 27, IBM Corp., Armonk, NY).

### 2.4 Ethical approval

The study protocol was approved by the institutional review board (7145-20-SMC, September 30, 2020)

## RESULTS

Overall, 1022 women met inclusion criteria, of whom 89 (8.7%) had IOL at 39\(\frac{0}{7}\)-39\(\frac{6}{7}\) weeks and 933 (91.3%) had LAC at ≥40\(\frac{0}{7}\).
Median cervical dilation at IOL group was 1 cm (interquartile range [IQR] 0.5–2 cm) and median cervical effacement at IOL was 70 (IQR 60–80 cm). Methods for IOL at 39 weeks were as follows: oxytocin \( n = 42 \) (47.2%), extraamniotic balloon \( n = 28 \) (31.5%) and amniotomy \( n = 19 \) (21.3%).

Table 1 presents a comparison of the study groups.

### 3.1 Maternal characteristics

Mean maternal height was higher in the IOL as compared to the LAC at ≥40 weeks group (162 vs. 163 cm, \( P = 0.019 \)), and maternal gestational weight gain was lower in the IOL group (12 vs. 13 kg, \( P = 0.013 \)). The proportion of women with diabetic disorders and hypertensive disorders was higher in the IOL group compared to the LAC at ≥40 weeks group (16.9% vs. 4.7% and 6.7% vs. 1.6%, \( P < 0.001 \) and \( P = 0.001 \), respectively).

### 3.2 Previous cesarean section characteristics

Mean gestational age at previous CS was lower in the IOL group (37 \( 6/7 \) vs. 38 \( 4/7 \), \( P = 0.003 \)). Cervical dilation at previous CS was lower in the IOL group compared to the LAC at ≥40 weeks group (mean 3 cm vs. 4 cm, \( P = 0.021 \)).

### 3.3 LAC characteristics

Sonographic estimated fetal weight was lower in the IOL group (3139 vs. 3363 g, \( P < 0.001 \)).

The proportion of LACs with oxytocin administration at any time was higher in the IOL group (67.4% vs. 24.4%, \( P < 0.001 \)). The proportion of meconium-stained amniotic fluid was lower in the IOL amniotomy group (13.5% vs. 27.0%, \( P = 0.005 \)).

Table 2 presents maternal and neonatal outcomes for both study groups.

### TABLE 1 Characteristics of women undergoing LAC - induction of labor at 39 weeks versus expectant management

| Characteristics                        | Induction at 39 \( 0/7 \) - 39 \( 6/7 \). \( n = 89 \) | LAC at ≥ 40 \( 0/7 \). \( n = 933 \) | \( P \)-value |
|----------------------------------------|-------------------------------------------------------|-------------------------------------|--------------|
| Women                                  |                                                       |                                     |              |
| Age, years                             | 33 ± 4.1                                              | 32 ± 4.4                            | 0.667        |
| Immigrant                              | 13 (14.6%)                                            | 101 (13.6%)                         | 0.785        |
| Body mass index, pre-delivery, kg/m\(^2\)| 28.0 ± 4.1                                            | 28.4 ± 4.2                          | 0.460        |
| Height, cm                             | 162 ± 6.3                                             | 163 ± 6.1                           | 0.019        |
| Weight gain, kg                        | 12 ± 5.6                                              | 13 ± 4.6                            | 0.013        |
| Smoking                                | 3 (3.4%)                                              | 32 (3.4%)                           | > 0.99       |
| Diabetic disorder                      | 15 (16.9%)                                            | 44 (4.7%)                           | < 0.001      |
| Hypertensive disorder                  | 6 (6.7%)                                              | 15 (1.6%)                           | 0.001        |
| Previous delivery                      |                                                       |                                     |              |
| Gestational age at Cesarean section, weeks | 37 \( 6/7 \) ± 2 \( 2/7 \)                           | 38 \( 6/7 \) ± 2 \( 3/7 \)           | 0.003        |
| Indication for Cesarean section        |                                                       |                                     | 0.825        |
| Arrest of labor                        | 28 (31.5%)                                            | 283 (30.3%)                         | 0.130        |
| Elective Cesarean section              | 24 (27.0%)                                            | 188 (20.2%)                         |              |
| Cervical dilation at delivery, cm      | 3 ± 2.8                                               | 4 ± 3.6                             | 0.021        |
| Second stage                           | 2 (2.2%)                                              | 68 (7.3%)                           | 0.079        |
| Birthweight, grams                     | 2879 ± 624                                            | 3071 ± 617                          | 0.006        |
| Current gestation                      |                                                       |                                     |              |
| Gestational age at LAC, weeks          | 39 \( 2/7 \) ± 0 \( 2/7 \)                           | 40 \( 1/7 \) ± 0 \( 4/7 \)           | < 0.001      |
| Sonographic estimated fetal weight, grams | 3139 ± 334                                          | 3363 ± 335                          | < 0.001      |
| Inter-delivery interval, years         | 3 ± 0.6                                               | 2 ± 0.6                             | 0.343        |
| Oxytocin administration                | 60 (67.4%)                                            | 228 (24.4%)                         | < 0.001      |
| Epidural analgesia                     | 78 (87.6%)                                            | 752 (80.6%)                         | 0.104        |
| Meconium-stained amniotic fluid        | 12 (13.5%)                                            | 252 (27.0%)                         | 0.005        |
| Intrapartum temperature > 38.0°C       | 3 (3.4%)                                              | 18 (1.9%)                           | 0.419        |

Note: Data are presented as number (%) or mean ± standard deviation.

Abbreviation: LAC, labor after cesarean section.
3.4 | LAC success

LAC success rate did not differ between study groups ($P = 0.138$), with unplanned CS rates of 34.8% in the IOL group and 27.4% in the LAC at ≥40 weeks group. The modes of vaginal deliveries or unplanned CS indications did not differ between groups either.

3.5 | Maternal outcome

There were three uterine ruptures (3.4%) in the IOL group and 11 (1.2%) in the LAC at ≥40 weeks group ($P = 0.115$). The rate of composite maternal outcomes occurrence was higher in the IOL group (18.0% vs. 10.1%, $P = 0.022$).

3.6 | Neonatal outcomes

Birthweight was lower in the IOL group compared to the LAC at ≥40 weeks group ($P < 0.001$), and the rate of macrosomia was lower ($P = 0.011$). Mean length of stay was longer in the IOL group (5 vs. 4 days, $P = 0.021$). The composite neonatal outcome rate was comparable between groups ($0.186$).
in the IOL at 39 weeks ($P = 0.003$). Uterine rupture was 3.4% (3/89) versus 1.1% (2/188) in the IOL at 39 and ≥40 weeks respectively ($P = 0.332$). Macrosomia rate was lower in the IOL at 39 weeks group (0% vs. 6.9%, $P = 0.011$). Other maternal and neonatal outcomes were comparable in both groups.

4 | DISCUSSION

In this study, IOL at 39 weeks among women undergoing LAC was not associated with improved neonatal outcomes as compared to expectant management. The mode of delivery was similar in both groups as well, however, the composite of adverse maternal outcome was higher in the IOL at 39 weeks group. In the sub-analysis of IOL at 39 weeks versus IOL beyond 39 weeks, adverse outcomes were comparable between our study groups.

It has become clearer that perinatal risk is not homogenous across the term gestational age range, and defining the optimal timing of delivery, especially in nulliparous, has gained interest in obstetrics. Generally, the most recent literature concludes that IOL at term compared with expectant management is associated with fewer neonatal deaths and a decrease in CS,18 although the optimal timing of IOL still requires further investigation.

### Table 3. Multivariate regression analysis of factors associated with composite adverse maternal outcome

| Characteristics                        | Adjusted odds ratio (95% Confidence interval) | $P$-value |
|----------------------------------------|-----------------------------------------------|-----------|
| Induction of labor                     | 1.95 (1.03–3.68)                              | 0.039     |
| Maternal age                           | 1.02 (0.97–1.07)                              | 0.479     |
| Body mass index before delivery        | 1.07 (1.03–1.12)                              | 0.002     |
| Diabetes mellitus                      | 0.97 (0.43–2.21)                              | 0.945     |
| Hypertensive disorders                 | 0.32 (0.04–2.43)                              | 0.267     |

Abbreviation: LAC, labor after cesarean section.

### Table 4. LAC outcomes of women and neonates- induction of labor at 39 weeks versus induction of labor at ≥40 weeks

| Characteristics                                      | Induction at 39⁰±7, $n = 89$ | Induction at ≥40⁰±7, $n = 188$ | $P$-value |
|------------------------------------------------------|-------------------------------|---------------------------------|-----------|
| Meconium-stained amniotic fluid                      | 12 (13.5%)                    | 56 (29.8%)                      | 0.003     |
| Intrapartum temperature > 38.0°C                     | 3 (3.4%)                      | 7 (3.7%)                        | >0.99     |
| Mode of delivery                                     |                               |                                 |           |
| Spontaneous                                          | 43 (48.3%)                    | 90 (47.9%)                      | 0.935     |
| Vacuum                                               | 14 (15.7%)                    | 27 (14.4%)                      |           |
| Forceps                                               | 1 (1.1%)                      | 4 (2.1%)                        |           |
| Cesarean section                                     | 31 (34.8%)                    | 67 (35.6%)                      | 0.896     |
| Maternal outcomes                                    |                               |                                 |           |
| Uterine rupture                                      | 3 (3.4%)                      | 2 (1.1%)                        | 0.332     |
| Postpartum hemorrhage                                | 7 (8.1%)                      | 12 (6.5%)                       | 0.617     |
| Length of stay >4 days                               | 8 (9.0%)                      | 16 (8.5%)                       | >0.99     |
| Composite maternal outcome                           | 16 (18.0%)                    | 28 (14.9%)                      | 0.512     |
| Newborns                                             |                               |                                 |           |
| Macrosomia                                           | 0 (0%)                        | 13 (6.9%)                       | 0.011     |
| Weight centile                                       | 54 ± 26                       | 57 ± 24                         | 0.369     |
| Apgar 1 minute <5                                    | 2 (2.2%)                      | 3 (1.6%)                        | 0.658     |
| Apgar 5 minute <7                                    | 0 (0%)                        | 1 (0.5%)                        | >0.99     |
| pH arterial <7                                       | 1 (1.1%)                      | 1 (0.5%)                        | 0.540     |
| Base excess ≥12 mEQ                                   | 1 (1.1%)                      | 1 (0.5%)                        | 0.540     |
| Neonatal intensive care unit admission               | 2 (2.2%)                      | 4 (2.1%)                        | >0.99     |
| Mechanical ventilation                               | 1 (1.1%)                      | 1 (0.5%)                        | 0.369     |
| Hypoxic ischemic encephalopathy                      | 0 (0%)                        | 1 (0.5%)                        | >0.99     |
| Length of stay, days                                 | 5 ± 2.4                       | 4 ± 2.0                         | 0.414     |
| Composite neonatal outcome                           | 9 (10.1%)                     | 17 (9.0%)                       | 0.826     |

Abbreviation: LAC, labor after cesarean section.
While this may be the conclusion of randomized controlled trials and meta-analysis,3,4,18 those who have excluded women with a previous CS undergoing a LAC. IOL in LAC is challenging both for the obstetrician and parturient and timing of IOL in LAC is understudied regarding maternal and neonatal outcomes. The question whether the effect of IOL at 39 weeks is evident also in LAC remains unanswered.

A previous study comparing IOL in LAC to expectant management at three time points at term, found no difference in neonatal outcomes between the comparison groups at each gestational age, in line with our results.14 However, that study included 39.9%–56.8% women with a prior vaginal delivery. Therefore, the inherent risk for adverse outcomes may have been lower as compared to our study, and counseling for women contemplating LAC with no prior vaginal delivery based on that must include this limitation.29 Although our study results show no statistical difference in neonatal outcomes between IOL and expectant management, we suggest that this could be probably due to sample size limitation, and possibly larger cohort might underline some difference. However, gathering a cohort of IOL at 39 in LAC with no prior vaginal delivery should probably be considered in a multi-center setting. Interestingly, while macrosomia is not considered an adverse outcome, it was more frequent in the expectant management group, and consideration should be given to this issue at LAC.

Regarding maternal outcomes, a recent study that compared IOL at 39 weeks to expectant management in LAC demonstrated similar results to our study – an increase in composite maternal morbidity in the IOL group.21 However, parity, a pivotal determinant of LAC, was not accounted for in that study.

We demonstrate that the rate of maternal composite adverse outcome was higher in the IOL group at 39 weeks compared to expectant management, and IOL remained an independent risk factor for adverse outcome following a multivariable analysis. Importantly, a previous large study has found higher rates of adverse maternal outcomes when comparing IOL at 39 weeks to expected management, concurrent with our results.25 Again, parity and prior vaginal delivery was not reported in that study. Furthermore, gestational age at delivery in the expectant management group was more frequent in the IOL group. Therefore, a meaningful clinical comparison of IOL and expectant management was somewhat questionable.

We found a 3.4% uterine rupture rates in the IOL group, which did not differ significantly from the expectant management group. Despite this, the absolute number of uterine ruptures was low (three cases). In the study by Palatnik et al., the rate of uterine rupture was higher in the IOL group at 390/7–399/7 (1.4%) as compared to a > 393/7 group (0.5%). The lower rate of uterine rupture in that study compared with our results, may be explained by the high proportion of women with prior vaginal deliveries in that study, significantly reducing the risk of this adverse event.25 A population-based study from Scotland, including women undergoing LAC with no prior vaginal delivery, found lower rates of uterine rupture compared to our results in an IOL at 39 weeks group (0.63%).24 Importantly, data for that study was collected during 1981–2007, and participants’ comorbidities were largely unreported, limiting the generalizability of that study for current clinical practice.

We included the length of hospital stay after delivery as one of the components of the maternal composite outcome. While this outcome may have psychological and financial effect, its long-term impact may be lower than the other two composite components. Thus, the overall negative effect of IOL at 39 weeks on maternal outcome may be less meaningful clinically considering this component. Of note, hospitalization length was similar in both groups in the 39 versus ≥40 weeks IOL comparison and longer than the expectant management group. This information should be taken in consideration when considering IOL in LAC at term.

LAC success rate in our study is comparable to the rate reported by Palatnik et al., despite a high proportion of women with prior vaginal deliveries in that study.19 Interestingly, LAC success rate are not similar in other studies. In the study by Stock et al., the rate of unplanned CS was lower in the IOL at 39 weeks group compared with expectant management (37.9% vs. 45.8%).24 In contrast, another study found higher rate of unplanned CS in an IOL at 39 weeks group compared with an expectant management group (45.6% vs. 29.8%, respectively). Of note, the IOL group in our study had significantly higher rates of diabetes mellitus and hypertensive disorders. This difference between the study groups may introduce bias to the study. We suggest that future studies exclude conditions that may require earlier IOL at term as routine care to minimize this source of bias.

Our study has some limitations. The main limitation is its retrospective design carrying inherent bias including selection and information bias. The possibility that unstudied factors had an effect on the results cannot be overlooked. A second notable caveat is the limited sample size, underpowered to evaluate statistical significance for rare maternal and neonatal outcomes. It is possible that a larger sample size would have led to statistical differences between groups. Third, we could not report the time interval from IOL to delivery, an important outcome in some studies. However, our study does have several strengths. The main strength of our study is the inclusion of women with no prior vaginal deliveries, thereby minimizing bias introduced by a favorable LAC profile for women who gave vaginal birth before. Moreover, women with no prior vaginal delivery may be more similar to nulliparous women, previously included in IOL studies including the ARRIVE trial. Of note, cervical parameter studied was subjective rather than objective sonographic measurement of cervical length. Finally, we included only safe methods of IOL in the study, contributing to the generalizability of the results. IOL with prostaglandins, which is associated with increased risk of uterine rupture,25 is not performed in our center among women undergoing LAC.

## Conclusion

In summary, IOL at 39 weeks of gestation among women undergoing LAC with no prior vaginal delivery is not associated with improved neonatal outcomes as compared to expectant management.
However, it may be associated with an increase in adverse maternal outcomes. Women undergoing medically indicated IOL following CS should be made aware of the increase in maternal risks related to the induction. Our results may serve as a decision support tool among women undergoing LAC when IOL is considered.

AUTHOR CONTRIBUTIONS
GL and RM reviewed the literature, collected data and wrote the paper.

CONFLICTS OF INTEREST
None.

DATA AVAILABILITY STATEMENT
No. Research data are not shared.

ORCID
Raanan Meyer https://orcid.org/0000-0002-0720-4343

REFERENCES
1. Grobman WA, Caughey AB. Elective induction of labor at 39 weeks compared with expectant management: a meta-analysis of cohort studies. Am J Obstet Gynecol. 2019;221(4):304–310. doi:10.1016/j.ajog.2019.02.046
2. Souter V, Painter I, Sitcov K, Caughey AB. Maternal and newborn outcomes with elective induction of labor at term. Am J Obstet Gynecol. 2019;220(3):273.e1–273.e11. doi:10.1016/j.ajog.2019.01.223
3. Grobman WA, Rice MM, Reddy UM, et al. Labor induction versus expectant management in low-risk nulliparous women. N Engl J Med. 2018;379(6):513–523. doi:10.1056/NEJMoa1800566
4. Walker KF, Bugg GJ, Macpherson M, et al. Randomized trial of labor induction in women 35 years of age or older. N Engl J Med. 2016;374(9):813–822. doi:10.1056/NEJMoa1509117
5. ACOG Practice Bulletin No. 205: vaginal birth after cesarean delivery. Obstet Gynecol. 2019;133(2):e110–e127. doi:10.1097/AOG.0000000000003078
6. Royal College of Obstetricians & Gynaecologists. Birth after Previous Caesarean Birth (Green-top Guideline No. 45). Second edition. October 2015.
7. McMahon MJ, Luther ER, Bowes WA, Olshan AF. Comparison of a trial of labor with an elective second cesarean section. N Engl J Med. 1996;335(10):689–695. doi:10.1056/NEJM199609053351001
8. Cahill AG, Stamilio DM, Odibo AO, et al. Is vaginal birth after cesarean (VBAC) or elective repeat cesarean safer in women with a prior vaginal delivery? Am J Obstet Gynecol. 2006;195(4):1143–1147. doi:10.1016/j.ajog.2006.06.045
9. Landon MB, Hauth JC, Leveno KJ, et al. Maternal and perinatal outcomes associated with a trial of labor after prior cesarean delivery. N Engl J Med. 2004;351(25):2581–2589. doi:10.1056/NEJMoa040405
10. Al-Ziori I, Daltveit AK, Forssén L, et al. Risk factors for complete uterine rupture. Am J Obstet Gynecol. 2017;216(2):165.e1–165.e8. doi:10.1016/j.ajog.2016.10.017

How to cite this article: Meyer R, Levin G. Maternal and perinatal outcome of induction at 39 weeks versus expectant management in labor after cesarean section. Int J Gynecol Obstet. 2022;159:480–486. doi: 10.1002/ijgo.14159