*Original Research*

# Maximum Oxytocin Dose and Uterine Rupture During Trial of Labor After Cesarean

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**OBJECTIVE:** To evaluate the association between maximum oxytocin dose and uterine rupture among individuals undertaking a trial of labor after cesarean (TOLAC). Secondarily, to evaluate the association between total time on oxytocin and time at maximum oxytocin dose and uterine rupture.

**METHODS:** We conducted a secondary analysis of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network Assessment of Perinatal Excellence study, an observational cohort of deliveries after 23 weeks of gestation across 25 U.S. hospitals from 2008 to 2011. Individuals with a singleton, cephalic, live fetus who had one prior cesarean delivery and were undertaking TOLAC, including those undergoing spontaneous, augmented, or induced labor, were included. Those with a contraindication to TOLAC or a fetus with an anomaly or known genetic abnormality were excluded. The exposure was intrapartum oxytocin dose in milli-international units per minute (milli-international units/min), assessed both categorically (0, 1–20, more than 20 milli-international units/min) and continuously. The primary outcome was uterine rupture. Secondary outcomes were vaginal birth after cesarean (VBAC), blood transfusion, and intensive care unit (ICU) admission. Trends in outcomes by oxytocin were assessed using the Cochran-Armitage trend test. Multivariable modeling estimated the association between maximum oxytocin dose (both as a categorical and continuous variable) and outcomes. The duration of any oxytocin, the duration at the maximum dose of oxytocin, and outcomes were assessed.

**RESULTS:** Of 5,201 individuals undergoing TOLAC, 3,406 (65.5%) received 0 milli-international units/min of oxytocin, 1,659 (31.9%) received 1–20 milli-international units/min, and 136 (2.6%) received more than 20 milli-international units/min. The majority of the cohort (n=3,391) entered spontaneous labor; 1,076 patients received augmentation and 733 were induced. The range of maximum oxytocin doses was 0–60 milli-international units/min. There were 37 cases of uterine rupture (0.7%, 95% CI, 0.5–0.9%). The frequency of uterine rupture by maximum oxytocin dose category was 0.2% (n=7) with no oxytocin (0 milli-international units/min), 1.6% (n=27) with an oxytocin dose of 1–20 milli-international units/min, and 2.2% (n=3) with oxytocin doses greater than 20 milli-international units/min. Higher maximum oxytocin doses were associated with a trend of an increase in uterine rupture ($P<.001$ Cochran-Armitage test of trend). In adjusted modeling, maximum oxytocin doses of 1–20 milli-international units/min and doses greater than 20 milli-international units/min were associated with uterine rupture (adjusted odds ratio [aOR] 8.82, 95% CI, 3.61–21.6; and aOR 11.0, 95% CI, 2.67–45.3, respectively), compared with 0 milli-international units/min; however, a higher maximum dose (more than 20 milli-international units/min) was not associated with uterine rupture (aOR 1.25, 95% CI, 0.37–4.22) when compared with a lower maximum dose of oxytocin (1–20 milli-international units/min). When analyzed as a continuous variable, a higher maximum oxytocin dose was associated with higher odds of uterine rupture (aOR 1.40 for each 5 milli-international units/min higher dose of oxytocin, 95% CI, 1.21–1.62) but also was associated with successful VBAC. Maximum oxytocin dose was not associated with blood transfusion or ICU admission. Longer duration of any intrapartum oxytocin and longer dura-

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**tion at maximum oxytocin dose also were associated with higher odds of uterine rupture.**

**CONCLUSION: Receipt of oxytocin at both lower and higher doses was associated with higher odds of uterine rupture across the full cohort when compared with no oxytocin exposure and also was associated with successful VBAC. Although a trend of increasing rupture with higher doses was observed, a maximum intrapartum higher dose (greater than 20 milli-international units/min) of oxytocin was not associated with uterine rupture when compared with lower dose. Thus, an upper safety threshold for maximum dose of oxytocin could not be identified.**

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The American College of Obstetricians & Gynecologists supports a trial of labor after cesarean (TOLAC), with a goal of vaginal birth after cesarean (VBAC) as a safe alternative to repeat cesarean delivery in appropriately selected and counseled individuals.[1] Although uterine rupture is a feared complication, with associated significant maternal and perinatal morbidity, the absolute risk is low, and overall data support the safety of TOLAC.[2–4] As a result, approximately one-quarter of individuals with a prior cesarean delivery opt to undertake TOLAC.[5]

Oxytocin is widely used for induction and augmentation of patients in the labor and delivery department, including those undertaking TOLAC.[1,6] Whether protocol modifications, such as a maximum dose or length of oxytocin exposure, should be made relative to patients without a prior cesarean delivery remains uncertain. In a retrospective multicenter cohort study of individuals undertaking TOLAC, Cahill et al[7] found an increased risk of uterine rupture among individuals reaching oxytocin levels greater than 20 milli-international units per minute as compared with lower doses. These findings have not been replicated nor have national guidelines changed.[1]

Therefore, we aimed to evaluate the association between maximum oxytocin dose and uterine rupture among individuals undertaking TOLAC by using data from an existing multicenter cohort study. Secondarily, we aimed to evaluate the association between total time on oxytocin and time at maximum oxytocin dose and uterine rupture.

## METHODS

This was a secondary analysis of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network's APEX (Assessment of Perinatal Excellence) study. The APEX study was an observational cohort of all deliveries after 23 weeks of gestation with a live fetus at hospital admission that occurred on randomly selected days from March 2008 to February 2011 at 25 U.S. hospitals. Trained perinatal research personnel completed data abstraction for the maternal–neonatal dyads that included demographics, medical and obstetric history, intrapartum course, and postpartum outcomes. The parent study was approved by the institutional review board of each participating institution under a waiver of consent. The full study protocol and results have been published previously.[8,9]

This analysis included individuals with a singleton, cephalic, live fetus who undertook TOLAC, including those undergoing spontaneous, augmented, or induced labor. Individuals with more than one prior cesarean delivery; history of myomectomy; or history of classical, reverse T or J uterine incision were excluded. Individuals with pregnancies complicated by known fetal or genetic abnormalities also were excluded.

The exposure was maximum intrapartum oxytocin dose (in milli-international units/min). For analyses, maximum oxytocin dosage was assessed in two ways: 1) maximum oxytocin dose was considered categorically as 0 milli-international units/min, 1–20 milli-international units/min, or greater 20 milli-international units/min; and 2) maximum oxytocin dose was considered as a continuous variable.

The primary outcome was uterine rupture. Secondary outcomes included VBAC, any blood transfusion, and intensive care unit (ICU) admission. All outcomes were evaluated during the delivery hospitalization.

Baseline characteristics were compared among the three oxytocin dose categories (0 milli-international units/min, 1–20 milli-international units/min, and more than 20 milli-international units/min) using analysis of variance for continuous variables and $\chi^2$ or Fisher exact tests for categorical variables. The demographics and baseline characteristics assessed included maternal age; maternal race and ethnicity; insurance type; body mass index (BMI, calculated as weight in kilograms divided by height in meters squared from the most recent pregnancy weight), comorbid health conditions such as pregestational diabetes, gestational diabetes, and chronic hypertension; and hypertensive disorders of pregnancy. The pregnancy and labor characteristics assessed included the type of labor (spontaneous, spontaneous with augmentation, or induced), intrauterine pressure catheter use, neonatal birth weight,

neuraxial anesthesia use, gestational age at delivery, and history of vaginal delivery. *Duration of labor* was defined as the time from admission to labor and delivery to either the time of delivery or the time of the decision to perform cesarean delivery.

The rate of the primary outcome was reported with 95% CIs. In univariable analysis, differences in uterine rupture by category of maximum oxytocin dose were reported. Trends in outcomes by oxytocin were assessed using the Cochran-Armitage trend test. Using logistic regression models, the association between maximum oxytocin dose (both as a categorical and continuous variable) and outcomes was assessed. Modeling was adjusted for prior vaginal delivery and BMI. These were selected a priori as relevant confounders based on existing literature on their association with VBAC and uterine rupture.[10,11] Additional characteristics that differed (by $P<.05$) in univariable comparisons were considered for multivariable models.

In exploratory analyses, we assessed the relationships among the duration of any oxytocin exposure, the duration at maximum dose of oxytocin, and uterine rupture. Time on any dose of oxytocin was calculated in minutes (min). *Duration of any oxytocin exposure* was defined from oxytocin initiation through cessation of oxytocin (ie, oxytocin stop time), the time of the decision to proceed with cesarean delivery, or the delivery time. Patients without any oxytocin exposure were included with a time on oxytocin of 0 minutes. The total time on the maximum oxytocin dose also was calculated in minutes. Individuals without oxytocin exposure were included, with a time of 0 minutes on the maximum oxytocin dose. A sensitivity analysis was performed, limiting the population to those with induction of labor and those who received oxytocin.

Because this was a secondary analysis of an observational cohort, the results should be considered exploratory. No adjustments were made for multiple comparisons. $P<.05$ was considered statistically significant. Imputation for missing data was not performed. All analyses were completed using SAS 9.4. Reporting follows the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for observational studies.[12]

## RESULTS

Of 5,201 individuals in the study who underwent TOLAC (Fig. 1), 3,406 (65.5%) received no oxytocin, 1,659 (31.9%) received 1–20 milli-international units/min of oxytocin, and 136 (2.6%) received more than 20 milli-international units/min of oxytocin. Maximum oxytocin doses ranged from 0–60 milli-international units/min. Overall, 3,391 patients entered spontaneous labor, 1,076 were augmented with oxytocin, and 733 were induced. Baseline characteristics for the cohort differed by maximum oxytocin dose (Table 1).

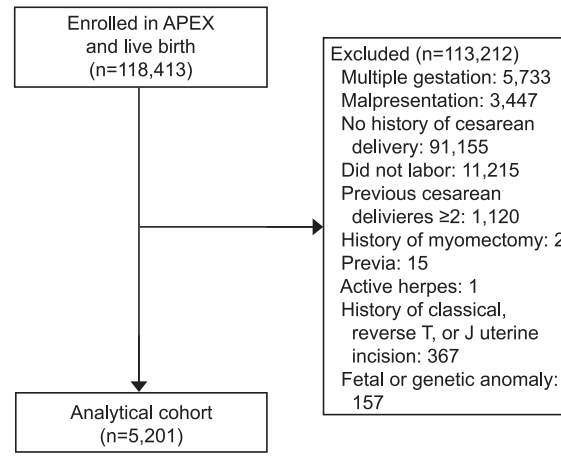


**Fig. 1.** Study population. APEX, Assessment of Perinatal Excellence.

*Bruno. Oxytocin Dose and Uterine Rupture. Obstet Gynecol 2025.*

There were 37 uterine rupture events (0.7%, 95% CI, 0.5–0.9%). The frequency of uterine rupture by maximum oxytocin dose category was 0.2% (n=7) with no oxytocin (0 milli-international units/min), 1.6% (n=27) with maximum oxytocin doses of 1–20 milli-international units/min, and 2.2% (n=3) with maximum oxytocin doses greater than 20 milli-international units/min. Higher maximum oxytocin doses (categories: 0, 1–20, more than 20 milli-international units/min) were associated with a trend of increased uterine rupture and VBAC ($P<.001$ from Cochran-Armitage test of trend), but were not associated with an increased trend in blood transfusion ($P=.077$) or ICU admission ($P=.090$).

In adjusted modeling, maximum oxytocin doses that ranged from 1–20 milli-international units/min (0.2% vs 1.6%, adjusted odds ratio [aOR] 8.82) and doses greater than 20 milli-international units/min (95% CI, 3.61–21.6; and 0.2% vs 2.2%) were associated with higher odds of uterine rupture, compared with no oxytocin (aOR 11.0, 95% CI, 2.67–45.3). However, uterine rupture was not associated with oxytocin dose in the pairwise comparison of higher maximum oxytocin doses with lower maximum oxytocin doses (doses greater than 20 milli-international units/min vs doses that ranged from 1–20 milli-international units/min; aOR 1.25, 95% CI, 0.37–4.22; Appendix 1, available online at http://links.lww.com/AOG/E394).

**Table 1. Baseline Characteristics of the Study Population by Oxytocin Maximum Dose**

| Characteristic* | Oxytocin Maximum Dose (milli-international units/min) | | | $P^{\dagger}$ |
|---|---|---|---|---|
| | 0 (n=3,406) | 1–20 (n=1,659) | Greater Than 20 (n=136) | |
| Maternal age (y) | 29.7±5.8 | 29.5±5.8 | 28.7±5.6 | .081 |
| Race and ethnicity | | | | <.001 |
| Hispanic | 1,099 (32.3) | 450 (27.1) | 35 (25.7) | |
| Non-Hispanic Asian | 217 (6.4) | 70 (4.2) | 3 (2.2) | |
| Non-Hispanic Black | 674 (19.8) | 434 (26.2) | 65 (47.8) | |
| Non-Hispanic White | 1,247 (36.6) | 586 (35.3) | 28 (20.6) | |
| None of the above | 136 (4.0) | 98 (5.9) | 4 (2.9) | |
| Missing | 33 (1.0) | 21 (1.3) | 1 (0.7) | |
| Insurance type | | | | <.001 |
| Private | 1,503 (44.5) | 632 (38.5) | 34 (25.4) | |
| Government assisted | 1,370 (40.6) | 851 (51.9) | 79 (59.0) | |
| Self-pay | 503 (14.9) | 157 (9.6) | 21 (15.7) | |
| BMI ($kg/m^2$) | | | | <.001 |
| Lower than 25 | 359 (10.8) | 139 (8.6) | 7 (5.3) | |
| 25–29.9 | 1,177 (35.5) | 507 (31.3) | 30 (22.7) | |
| 30–34.9 | 1,061 (32.0) | 502 (31.0) | 37 (28.0) | |
| 35–39.9 | 456 (13.8) | 263 (16.2) | 26 (19.7) | |
| 40 or higher | 260 (7.8) | 209 (12.9) | 32 (24.2) | |
| Comorbid health conditions | | | | |
| Chronic hypertension | 65 (1.9) | 62 (3.7) | 20 (14.7) | <.001 |
| HDP | 102 (3.0) | 107 (6.4) | 34 (25.0) | <.001 |
| Pregestational diabetes | 48 (1.4) | 24 (1.4) | 8 (5.9) | <.001 |
| Gestational diabetes | 246 (7.2) | 119 (7.2) | 13 (9.6) | .565 |
| Prior vaginal delivery | 1,418 (41.6) | 559 (33.7) | 46 (33.8) | <.001 |
| Gestational age at delivery (wk) | | | | <.001 |
| Less than 37 | 482 (14.2) | 147 (8.9) | 16 (11.8) | |
| 37–38 | 1,368 (40.2) | 411 (24.8) | 40 (29.4) | |
| 39–40 | 1,425 (41.8) | 911 (54.9) | 57 (41.9) | |
| 41 or more | 131 (3.8) | 190 (11.5) | 23 (16.9) | |
| Neuraxial anesthesia use | 1,484 (48.9) | 1,493 (92.9) | 121 (89.6) | <.001 |
| Labor type | | | | <.001 |
| Spontaneous | 3,342 (98.1) | 48 (2.9) | 1 (0.7) | |
| Spontaneous, augmented | 5 (0.1) | 1,040 (62.7) | 31 (22.8) | |
| Induced | 58 (1.7) | 571 (34.4) | 104 (76.5) | |
| Intrauterine pressure catheter use | 451 (13.2) | 910 (54.9) | 101 (74.3) | <.001 |
| Neonatal birth weight (g) | 3,248±585.1 | 3,323±550.5 | 3,271±588.5 | <.001 |

BMI, body mass index; HDP, hypertensive disorders of pregnancy.
Data are mean±SD or n (%) unless otherwise specified.
* Data were missing for insurance type (n=51), BMI (n=136), chronic hypertension (n=2), pregestational diabetes (n=7), gestational diabetes (n=87), neuraxial anesthesia use (n=427), type of labor (n=1), and intrauterine pressure catheter use (n=1).
† *P* value from $\chi^2$ for categorical characteristics and analysis of variance for continuous measures.

A maximum oxytocin dose of 1–20 milli-international units/min and maximum doses greater than 20 milli-international units/min were associated with VBAC in unadjusted and adjusted models when compared with no oxytocin (Table 2). In pairwise comparison, a higher maximum dose of oxytocin was associated with lower odds of VBAC when compared with a lower maximum dose of oxytocin (Appendix 1, http://links.lww.com/AOG/E394). Blood transfusion was not associated with oxytocin dose when compared with no oxytocin (Table 2) nor in the higher compared with lower pairwise comparison. Overall, ICU admission was rare across all maximum oxytocin doses: 0.4% for doses of 0 milli-international units/min (n=15); 1.0% for doses ranging from 1–20 milli-international units/min (n=17); and 0% for doses greater than 20 milli-international units/min (n=0). When the maximum oxytocin dose was analyzed as a continuous variable, there was an increased odds of uterine rupture for every 5-milli-international units/min oxytocin dose increase in an unadjusted model (OR 1.42, 95% CI, 1.24–1.63) and in an adjusted model (aOR 1.40, 95% CI, 1.21–1.62; Appendix 2, available online at http://links.lww.com/AOG/E394).

**Table 2. Primary and Secondary Outcomes by Maximum Dose of Oxytocin Intrapartum Among Individuals Undertaking Trial of Labor After Cesarean***

| Oxytocin Maximum Dose (milli-international units/min) | Frequency (%) | Trend $P^{\dagger}$ | Unadjusted OR (95% CI) | Adjusted OR (95% CI)$^{\ddagger}$ |
|---|---|---|---|---|
| Uterine rupture | | | | |
| 0 (n=3,406) | 7 (0.2) | <.001 | Ref | Ref |
| 1–20 (n=1,659) | 27 (1.6) | | 8.03 (3.49–18.5) | 8.82 (3.61–21.6) |
| Greater than 20 (n=136) | 3 (2.2) | | 11.0 (2.80–42.8) | 11.0 (2.67–45.3) |
| VBAC | | | | |
| 0 (n=3,406) | 1,464 (43.0) | <.001 | Ref | Ref |
| 1–20 (n=1,659) | 1,201 (72.4) | | 3.48 (3.06–3.95) | 3.55 (3.11–4.07) |
| Greater than 20 (n=136) | 80 (58.8) | | 1.90 (1.34–2.68) | 2.28 (1.57–3.32) |
| Any blood transfusion | | | | |
| 0 (n=3,406) | 54 (1.6) | .077 | Ref | Ref |
| 1–20 (n=1,659) | 36 (2.2) | | 1.38 (0.90–2.11) | 1.26 (0.81–1.95) |
| Greater than 20 (n=136) | 4 (2.9) | | 1.88 (0.67–5.27) | 1.27 (0.44–3.71) |
| ICU admission | | | | |
| 0 (n=3,406) | 15 (0.4) | .090 | — | — |
| 1–20 (n=1,659) | 17 (1.0) | | — | — |
| Greater than 20 (n=136) | 0 (0) | | — | — |

OR, odds ratio; VBAC, vaginal birth after cesarean; ICU, intensive care unit.
* Final adjusted models included 5,065 patients from 5,201 records after excluding for missing variables.
† *P* from Cochran-Armitage trend test.
‡ All models adjusted for prior vaginal delivery and body mass index (BMI) 40 or higher. Models for VBAC and blood transfusion additionally adjusted for gestational age at delivery 40 weeks or more and any hypertension. Modeling was not done for ICU admission secondary to no events in the group that received more than 20 milli-international units/min of oxytocin.

In exploratory analysis, the total duration of any oxytocin intrapartum ranged from 0 minutes to 52 hours, and the total duration at maximum oxytocin dose intrapartum ranged from 0 minutes to 51 hours. Longer total duration of any oxytocin and total duration at maximum oxytocin dose were associated with a trend of increased uterine rupture ($P<.001$ from Cochran-Armitage test of trend). For longer duration of any intrapartum oxytocin, the odds of uterine rupture increased in unadjusted and adjusted analyses (OR 1.11 per 1 hour of oxytocin, 95% CI, 1.07–1.14; aOR 1.11, 95% CI, 1.07–1.15; Fig. 2). Similarly, a longer duration of time at maximum oxytocin doses was associated with uterine rupture (Table 3).

In a sensitivity analysis, we limited the population to 1,795 individuals with any oxytocin exposure. In adjusted models, total dose of oxytocin with continuous parameterization was no longer associated with uterine rupture (for 5-unit incremental increase in oxytocin dose: aOR 1.09, 95% CI, 0.87–1.35; Appendix 2, http://links.lww.com/AOG/E394). The total duration of time on oxytocin and the duration at maximum oxytocin doses intrapartum remained significantly associated with uterine rupture (Appendix 3, available online at http://links.lww.com/AOG/E394). Similarly, in a sensitivity analysis limited to 733 people with labor induction, maximum dose of oxytocin was no longer significantly associated with

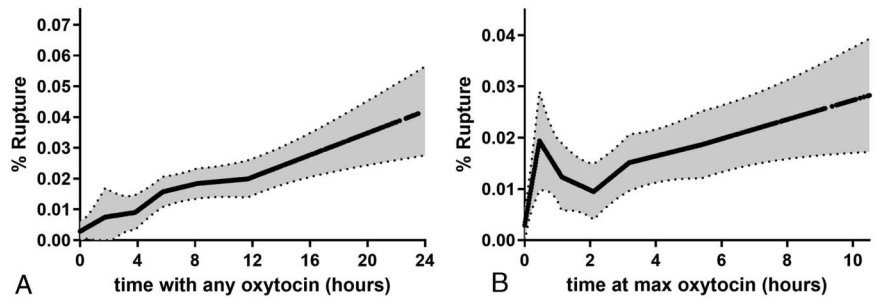


**Fig. 2.** Uterine rupture rate (%) by total duration on oxytocin and duration at maximum dose of oxytocin intrapartum among patients undertaking a trial of labor after cesarean. Percentage rupture is graphically summarized across time with any oxytocin (**A**) and time at maximum oxytocin (**B**) using locally estimated scatterplot smoothing, where each point was smoothed with the neighboring 40% of the data. Time on the x-axis is truncated at the 99th percentile.

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**Table 3. Uterine Rupture by Total Duration of Time on Oxytocin and Duration at Maximum Dose of Oxytocin Intrapartum Among Individuals Undertaking Trial of Labor After Cesarean***

| Outcome | Frequency (%) | Trend $P$† | OR (95% CI) for 1-h Incremental Difference | |
|---|---|---|---|---|
| | | | Unadjusted | Adjusted‡ |
| Total duration of oxytocin intrapartum | | | | |
| 0 min | 7/3,406 (0.2) | <.001 | 1.11 (1.07–1.14) | 1.11 (1.07–1.15) |
| 1–19 h | 17/1,313 (1.3) | | | |
| 20 h or more | 13/476 (2.7) | | | |
| Total duration at maximum oxytocin dose | | | | |
| 0 min | 7/3,410 (0.2) | <.001 | 1.14 (1.09–1.19) | 1.11 (1.05–1.16) |
| 1–9 h | 28/1,759 (1.6) | | | |
| 10 h or more | 2/15 (13.3) | | | |

OR, odds ratio.
* Number available in adjusted modeling was 5,060 patients for total duration of oxytocin and 4,694 patients for duration at maximum oxytocin dose.
† $P$ from Cochran-Armitage trend test.
‡ Adjusted for prior vaginal delivery, duration of labor, and body mass index (BMI) 40 or higher.

rupture (Appendix 2, http://links.lww.com/AOG/E394 oxytocin doses remained significantly associated (Appendix 3, http://links.lww.com/AOG/E394); rupture in this subgroup was too infrequent for adjusted modeling.

## DISCUSSION

In this secondary analysis of a multicenter cohort study, rates of uterine rupture were 0.2% for an oxytocin dose of 0 milli-international units/min, 1.6% for maximum oxytocin doses of 1–20 milli-international units/min, and 2.2% for maximum oxytocin doses greater than 20 milli-international units/min, with a trend of increasing uterine rupture rates by oxytocin maximum dose. Both higher and lower maximum doses of oxytocin were associated with uterine rupture among individuals undertaking TOLAC when compared with those with no oxytocin exposure; however, higher-dose oxytocin was not associated with uterine rupture when compared with lower-dose oxytocin. A higher maximum oxytocin dose was associated with VBAC but not blood transfusion when compared with no exposure. In exploratory analyses, a longer duration of time on any oxytocin and longer durations at maximum oxytocin doses intrapartum were associated with increased odds of uterine rupture. An upper safety threshold for a maximum oxytocin dose was not identified.

We found that the use of any oxytocin was associated with higher rates of VBAC across the full study population, which included individuals undergoing spontaneous, spontaneous augmented, and induced labor, when compared with no exposure. There are known benefits of achieving VBAC, such as reduced maternal morbidity and stopping the cycle of recurrent cesarean deliveries, with their downstream complications (eg, placenta accreta spectrum).[1,13] Therefore, defining a safety threshold for oxytocin maximum dosage or length of exposure to reduce uterine rupture risk also needs to balance the benefits of achieving VBAC.

In a prior planned secondary analysis of a multicenter retrospective cohort study that included 13,523 individuals undertaking TOLAC, Cahill et al[7] found a dose–response relationship between maximum intrapartum oxytocin dose and uterine rupture. Individuals receiving a maximum intrapartum oxytocin doses of 6–10 milli-international units/min, 11–20 milli-international units/min, and 21–30 milli-international units/min, compared with no intrapartum oxytocin exposure, experienced higher rates of uterine rupture: 1.3% for doses of 6–10 milli-international units/min (aOR 1.97, 95% CI, 1.15–3.37); 1.8% for doses of 11–20 milli-international units/min (aOR 2.62, 95% CI, 1.61–4.24); and 2.1% for doses of 21–30 milli-international units/min (aOR 2.98, 95% CI, 1.51–5.9). Our findings were similar, with higher maximum doses of oxytocin associated with higher odds of uterine rupture in unadjusted and adjusted models. However, in our analyses, higher maximum doses of oxytocin intrapartum were not associated with uterine rupture when compared with lower maximum doses of oxytocin intrapartum. Taken together, the findings highlight the need for further work to elucidate a potential upper-safety threshold of oxytocin dosage among individuals undertaking TOLAC.

Spontaneous labor without any oxytocin exposure among individuals undertaking TOLAC may reduce the risk of uterine rupture, but it is an

impractical solution. Many patients pursuing TOLAC may not have the opportunity to await spontaneous labor if a medical indication for delivery arises. Other patients may opt for elective induction, understanding the dearth of data to guide them on risks and benefits. Some observational studies have found that induction of labor among patients undertaking TOLAC was associated with higher VBAC success; therefore, this benefit may outweigh the small, absolute risk of uterine rupture for many patients.[10,13–16] Even patients who present in spontaneous labor may need augmentation with oxytocin. Therefore, further work is necessary to define safety parameters for a maximum oxytocin threshold and uterine rupture risk.

Notably, the higher oxytocin dosing associated with uterine rupture is likely indicative of dysfunctional labor. In analyses of individuals who received oxytocin, higher maximum doses of oxytocin were associated with lower odds of VBAC when compared with lower maximum doses of oxytocin (58.8% vs 72.4%; aOR 0.64, 95% CI, 0.44–0.94). We hypothesize that the dysfunctional labor likely predisposes to uterine rupture rather than the oxytocin itself. Unfortunately, the associated tocodynamometer data around frequency and strength of contractions were unavailable and could not be assessed.

In exploratory analyses, longer length of time on any oxytocin and at maximum dose of oxytocin intrapartum were associated with increased odds of uterine rupture. Beyond a threshold for maximum oxytocin dose, time of exposure to oxytocin is likely an important component.[17] In the prior work by Cahill et al[7] and in this study, the starting oxytocin dosage and oxytocin escalation protocol (ie, a high-dose oxytocin titration vs low-dose oxytocin titration) were not known. These may be important factors in defining uterine rupture risk among individuals undertaking TOLAC. Prospective study with detailed oxytocin usage details such as initial dose, titration protocol (eg, length between dose increases, increment of dose increase), and pauses and resumptions in use would help inform safety thresholds as well as potential for optimization of VBAC.

This study has several limitations. Granular details were unavailable for oxytocin protocols (ie, starting oxytocin dose or oxytocin titration protocol), cervical examinations, time in latent and active phases of labor, and Bishop score across deliveries and hospitals. The parent study period was from 2008 to 2011; results may not reflect current obstetric practice around oxytocin titration among individuals undertaking TOLAC. However, the American College of Obstetricians & Gynecologists' guidelines have not changed in that interval, reflecting the absence of evidence to inform this practice. Perinatal outcomes were outside the scope of the current study but are assuredly valuable in the risk and benefit considerations. Despite a large sample size, the evaluated outcomes are rare events, and the lack of an association between maximum oxytocin dose and uterine rupture may represent type II error. In addition, there may be persistent confounding despite multivariable modeling. Higher doses of oxytocin across any labor type (spontaneous, augmented, induced) may reflect dysfunctional labor rather than a concern with oxytocin itself.

This study has several strengths. The included hospitals reflect the geographic diversity and care variations of the United States, increasing generalizability of findings. The large size of the APEX dataset allowed for the evaluation of a rare outcome.

In summary, we found an association between oxytocin use and uterine rupture; however, higher maximum oxytocin dose was not associated with uterine rupture when compared with lower maximum oxytocin dose. Thus, no maximum oxytocin threshold for safety was identified. Findings contribute to the ongoing clinical care and research agendas around improving care and optimizing outcomes for individuals undertaking TOLAC.

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