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Association between Neuraxial Labor Analgesia and Neonatal Morbidity after Operative Vaginal Delivery

A Retrospective Cross-sectional Study

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- National obstetric guidelines indicate that adequate analgesia is a prerequisite for operative vaginal delivery (vacuum- or forceps-assisted).
- Although more than 80% of operative vaginal deliveries in the United States are performed with neuraxial analgesia, the impact on neonatal outcomes remains unclear.

What This Article Tells Us That Is New

- In analyses of national birth certificates from 2017, composite neonatal morbidity (low Apgar scores, assisted ventilation, seizures, neonatal intensive care unit admission, or neonatal transfer to another facility) was more common among 106,845 parturients receiving neuraxial analgesia *versus* those without neuraxial anesthesia (unadjusted composite outcome rate of 11.3% *vs.* 8.9%; adjusted relative risk, 1.19).
- However, *post hoc* adjusted analyses focused on neonatal clinical outcomes (adjusted relative risk, 1.07; $P = 0.054$) or incorporating county of delivery information (adjusted relative risk, 1.09; $P = 0.014$) demonstrated questionable clinical or statistical significance.
- A neonatal benefit of neuraxial analgesia for operative vaginal deliveries was not observed. Confounding by indication bias is a relevant possibility.

ABSTRACT

Background: Up to 84% of women who undergo operative vaginal delivery receive neuraxial analgesia. However, little is known about the association between neuraxial analgesia and neonatal morbidity in women who undergo operative vaginal delivery. The authors hypothesized that neuraxial analgesia is associated with a reduced risk of neonatal morbidity among women undergoing operative vaginal delivery.

Methods: Using United States birth certificate data, the study identified women with singleton pregnancies who underwent operative vaginal (forceps- or vacuum-assisted delivery) in 2017. The authors examined the relationships between neuraxial labor analgesia and neonatal morbidity, the latter defined by any of the following: 5-min Apgar score less than 7, immediate assisted ventilation, assisted ventilation greater than 6 h, neonatal intensive care unit admission, neonatal transfer to a different facility within 24 h of delivery, and neonatal seizure or serious neurologic dysfunction. The authors accounted for sociodemographic and obstetric factors as potential confounders in their analysis.

Results: The study cohort comprised 106,845 women who underwent operative vaginal delivery, of whom 92,518 (86.6%) received neuraxial analgesia. The proportion of neonates with morbidity was higher in the neuraxial analgesia group than the nonneuraxial group (10,409 of 92,518 [11.3%] *vs.* 1,271 of 14,327 [8.9%], respectively; $P < 0.001$). The unadjusted relative risk was 1.27 (95% CI, 1.20 to 1.34; $P < 0.001$); after accounting for confounders using a multivariable model, the adjusted relative risk was 1.19 (95% CI, 1.12 to 1.26; $P < 0.001$). In a *post hoc* analysis, after excluding neonatal intensive care unit admission and neonatal transfer from the composite outcome, the effect of neuraxial analgesia on neonatal morbidity was not statistically significant (adjusted relative risk, 1.07; 95% CI, 1.00 to 1.16; $P = 0.054$).

Conclusions: In this population-based cross-sectional study, a neonatal benefit of neuraxial analgesia for operative vaginal delivery was not observed. Confounding by indication may explain the observed association between neuraxial analgesia and neonatal morbidity, however this dataset was not designed to evaluate such considerations.

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In the United States, operative vaginal delivery with forceps or vacuum accounts for 3.1% of all vaginal deliveries.[1] A key benefit of operative vaginal delivery is avoidance of an intrapartum cesarean delivery, which carries significant morbidity to the mother.[2] However, compared with spontaneous vaginal delivery, operative vaginal delivery is associated with increased neonatal risks (cephalohematoma, scalp laceration, fractures, and brachial plexus injury) and several maternal morbidities (perineal tears and anal

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sphincter injury).[3–6] Therefore, identifying approaches that mitigate the likelihood of these morbidities in women who undergo operative vaginal delivery is of clinical importance.

Guidelines from the American College of Obstetricians and Gynecologists indicate that adequate maternal analgesia is a prerequisite for operative vaginal delivery.[2] Neuraxial analgesia may be preferred because it is more effective than other modalities. Indeed, among women who underwent operative vaginal delivery in 27 U.S. states in 2008, neuraxial labor analgesia was used in 84% of all forceps deliveries and 77% of all vacuum deliveries.[7] In addition to the analgesic benefits of neuraxial analgesia, adequate pelvic muscle relaxation facilitated by neuraxial analgesia may allow optimal placement of the forceps or vacuum device, thereby potentially reducing the likelihood of neonatal injury and morbidity. However, it is unclear whether neuraxial analgesia is associated with a lower risk of neonatal morbidity after operative vaginal delivery. Given national efforts to decrease cesarean delivery rates,[8,9] methods that optimize outcomes for infants delivered by operative vaginal delivery are of clinical interest.

We conducted a population-based analysis of women in the United States who underwent operative vaginal delivery in 2017. We hypothesized that the use of neuraxial analgesia is associated with a reduced risk of neonatal morbidity in this population.

Materials and Methods

Study Population

In this population-based cross-sectional study, we analyzed United States birth certificate data from 2017. Deidentified birth certificate data are made publicly available by the United States Centers for Disease Control and Prevention,[10] thus our analysis was exempt from Stanford University Institutional Review Board review. All states use the 2003 revised United States Standard Certificate of Live Birth format, which comprises detailed demographic, medical, and obstetric information. For this study, we adhered to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

Birth facility staff enter data into the birth certificate according to clinical records and maternal surveys. Each birth certificate contains a checkbox to designate whether or not a woman received "epidural or spinal anesthesia during labor." The birth certificate does not contain information about the specific type of neuraxial analgesia (*i.e.*, epidural, spinal, combined-spinal epidural) or other information regarding other analgesic modalities (*e.g.*, systemic [oral or parenteral] opioids, inhaled nitrous oxide).

Our study population comprised women with nonanomalous singleton pregnancies who underwent vacuum- or forceps-assisted delivery (operative vaginal delivery). We excluded women who had a spontaneous vaginal delivery, cesarean delivery, noncephalic fetal presentation, out-of-hospital birth, as well as those missing data for mode of delivery or neuraxial analgesia use. Although American College of Obstetricians and Gynecologists guidelines during the study period discouraged vacuum extraction at less than 34 weeks' gestational age,[11] there are no contraindications for attempting operative vaginal delivery based on gestational age. Therefore, based on expert obstetric opinion (Y.B.), we set conservative gestational age limits for defining our study cohort (between 36^{+0} and 41^{+6} weeks' gestation). We used complete case analysis as the highest percentage of missing values among all covariates was 1.98% for prenatal care.

Exposure, Outcome, and Covariates

The main exposure was use of neuraxial labor analgesia. The primary outcome variable was composite neonatal morbidity. The primary outcome was established *a priori* (before data analysis) and was defined by the presence of any of the following: 5-min Apgar score less than 7, requirement for immediate assisted ventilation, assisted ventilation for more than 6 h, neonatal intensive care unit admission, neonatal transfer to a different facility within 24 h of delivery, and neonatal seizure or serious neurologic dysfunction. Definitions of these birth certificate variables are published by the United States National Center for Health Statistics[12] and are available in Supplemental Digital Content 1 (http://links.lww.com/ALN/C489). Of note, the definition of a neonatal intensive care admission corresponds with the American Academy of Pediatrics designation of a level III or IV nursery.[13] We selected these outcomes based on literature review of studies reporting neonatal morbidity outcomes associated with operative vaginal delivery and data availability in the U.S. birth certificate dataset.[4,5,14–17]

The covariates included in our analysis were maternal age (less than 20, 20 to 34, 35 to 39, greater than or equal to 40 yr), education (less than high school, high school, any postsecondary), race/ethnicity (non-Hispanic White, non-Hispanic Black, non-Hispanic Asian, Hispanic, other), prepregnancy body mass index categorized using the World Health Organization classification[18] (underweight, normal, overweight, obese, obesity II, obesity III), trimester when prenatal care commenced (first, second, third, no prenatal care), insurance (Medicaid, private insurance, self-pay, other), prior livebirths (none, 1 or more), prior cesarean, preexisting or gestational diabetes, gestational hypertension or preeclampsia, induction of labor, labor augmentation, gestational age at delivery, and delivery location by U.S. Census region (Northwest, Midwest, South, and West).

Data Analysis

A data analysis and statistical plan was written after the data were initially accessed. Before primary data analysis, the main aims and analytic plan were reviewed by all study investigators in September 2019. Statistical analysis was performed with Stata Version 14.0 (StataCorp., USA). We performed descriptive analyses on characteristics of women with and without neuraxial analgesia. An uncorrected chi-square test was used to compare the frequencies

of categorical variables between the two groups. All analyses were performed using two-tailed hypothesis testing with a *P* value of less than 0.05 as statistically significant.

The association between neuraxial analgesia and neonatal morbidity was assessed using relative risk with 95% CI and was estimated by multivariable logistic regression with a binomial distribution and a log-link function.

Sensitivity Analyses

We performed several *a priori* sensitivity analyses to assess the robustness of our findings. Because evidence exists that vacuum extraction may be associated with an increased risk of neonatal trauma (*e.g.*, cephalohematoma, intracranial hemorrhage) compared to forceps delivery,[19] we performed stratified analysis to examine risk of neonatal morbidity among women who had forceps only and vacuum only. Additionally, because babies weighing greater than or equal to 4,000 g are at increased risk of newborn complications,[20] we performed a prespecified sensitivity analysis to assess the potential association between exposure and outcome in women with nonmacrosomic neonates by restricting the cohort to deliveries with neonates weighing less than 4,000 g.

A Priori Secondary Analyses

For the logistic models in our primary and sensitivity analyses, we examined crude and adjusted risk differences to quantify the magnitude of any increased or decreased risk associated with neuraxial analgesia.

Reviewer-requested *Post Hoc* Secondary and Sensitivity Analyses

During the peer review process, several *post hoc* secondary and sensitivity analyses were requested. First, survey data indicate that an in-house obstetric anesthesia service is more likely to be present in an urban hospital with a high obstetric volume than a low-volume rural hospital.[21,22] Further, perinatal outcomes, such as neonatal mortality and birth asphyxia are less prevalent in high-volume hospitals.[23,24] Therefore, it is plausible that hospitals with a dedicated or in-house obstetric anesthesia service are more likely to have a high-level neonatal intensive care unit and are less likely to arrange neonatal transfer. Based on this assumption, an association between neuraxial analgesia and neonatal morbidity may be explained, in part, by confounding by indication. To address this concern, we excluded neonatal intensive care unit admission and neonatal transport from our composite outcome, and then reanalyzed our estimates of risk associated with neuraxial analgesia using these revised criteria for the composite outcome (5-min Apgar score less than 7, requirement for immediate assisted ventilation, assisted ventilation for more than 6 h, neonatal seizure or serious neurologic dysfunction). Second, because the dataset contains information for the county of birth, we used generalized estimating equation models with a binomial family distribution and a logit link function to account for within-county clustering (1,568 counties in total). Third, we performed propensity score matching for the nonuse of neuraxial labor analgesia to an individual using neuraxial labor analgesia based on covariates included in the primary analysis, with one-to-one matching without replacement using nearest neighbor matching. Balance in maternal characteristics between women receiving *versus* not receiving neuraxial analgesia was assessed using absolute standardized difference, with less than 0.1 considered as acceptable balance. Within the propensity-matched cohort, we estimated the relative risk and 95% CI using our primary and revised composite outcome of neonatal morbidity.

Sample Size

We did not perform an *a priori* sample size estimation. However, before performing formal data analysis, we performed a power analysis using baseline data from our analytic sample. With 92,518 women with neuraxial analgesia and 14,327 women without neuraxial analgesia in our sample, an alpha of 0.05, power of 80%, and an assumed neonatal morbidity rate of 10% among women without neuraxial analgesia, the minimum detectable relative risk of neonatal morbidity for women without neuraxial analgesia compared to women with neuraxial analgesia was 1.09. Our sample size analysis did not include a minimum clinically significant effect size.

Results

We identified 3,864,754 livebirths in 2017 (fig. 1). We excluded 3,749,761 out-of-hospital births, cesarean deliveries, spontaneous vaginal deliveries, congenital anomalies, twins or multiple pregnancies, gestational age at delivery less than 36 weeks or greater than or equal to 42 weeks, breech presentation, and other or unknown fetal presentations. We also excluded 8,198 missing values for delivery location, delivery mode, neuraxial analgesia status, covariates, and neonatal morbidity (fig. 1). Our final analytic cohort comprised 106,845 women who underwent operative vaginal delivery of whom 92,518 (86.6%) received neuraxial analgesia.

Table 1 shows the patient characteristics of women who received and did not receive neuraxial analgesia. Compared to women without neuraxial analgesia, women with neuraxial analgesia were more likely to be non-Hispanic White, and have a secondary education, private insurance, no prior live births, preexisting or gestational diabetes, gestational hypertension or preeclampsia, induction of labor, augmentation of labor, initiated prenatal care in the first trimester, and delivered in the North, Midwest, or South census region.

Primary Outcome

The rate of composite neonatal morbidity was higher among women receiving neuraxial analgesia than those not receiving neuraxial analgesia (10,409 [11.3%] *vs.* 1,271

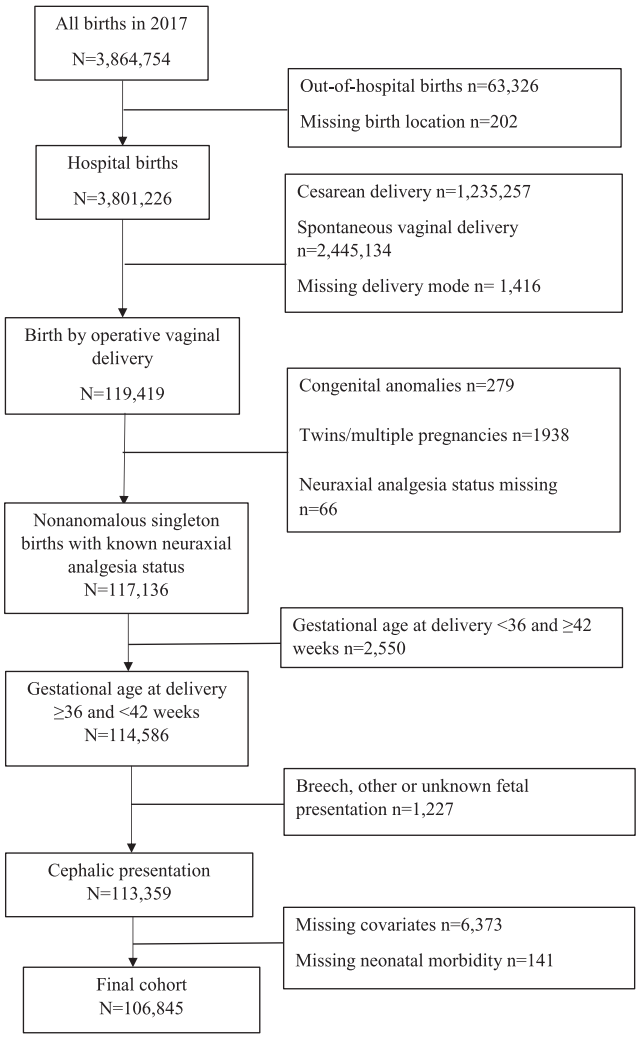

Fig. 1. Study flow chart.

[8.9%], respectively; $P < 0.001$). Table 2 shows the unadjusted and adjusted relative risk of neonatal morbidity. In the initial unadjusted analysis, the relative risk for neonatal morbidity was 1.27 (95% CI, 1.20 to 1.34; $P < 0.001$) in women with neuraxial analgesia compared to women without. The association was attenuated after adjusting for confounders (adjusted relative risk, 1.19; 95% CI, 1.12 to 1.26; $P < 0.001$).

Rates and risks of individual components of the composite neonatal morbidity outcome are presented in table 3. The three most frequent neonatal morbidities (in descending order) in both the neuraxial and no neuraxial analgesia groups were neonatal intensive care admission, immediate need for assisted ventilation, and 5-min Apgar scores less than 7.

Sensitivity Analyses

Table 2 presents the results of our models stratified according to the method of operative vaginal delivery (forceps or vacuum). In the forceps-assisted delivery cohort, compared to no neuraxial analgesia, women who received neuraxial analgesia had a 1.5-fold adjusted risk of neonatal morbidity. In the vacuum-assisted delivery cohort, neuraxial analgesia was associated with a 1.16-fold adjusted risk of neonatal morbidity. When the cohort was restricted to neonates weighing less than 4,000 g, results were similar to our main findings.

Secondary Analyses

Table 4 presents the unadjusted and the adjusted risk differences in the rate of composite neonatal morbidity according to presence or absence of neuraxial analgesia. For the original study cohort, the adjusted risk difference was 1.8 (95% CI, 1.2 to 2.3) per 100 deliveries. In our stratified analyses, the largest adjusted risk difference was observed among forceps deliveries (3.9 [95% CI, 2.5 to 5.2] per 100 deliveries).

Table 1. Patient Characteristics of Women Undergoing Operative Vaginal Delivery with and without Neuraxial Analgesia

Characteristic	No Neuraxial Labor Analgesia (n = 14,327)	Neuraxial Labor Analgesia (n = 92,518)	*P* Value
Maternal age, yr			< 0.001
< 20	1,001 (7.0)	6,771 (7.3)	
20–34	10,985 (76.7)	72,135 (78.0)	
35–39	1,932 (13.5)	11,285 (12.2)	
≥ 40	409 (2.8)	2,327 (2.5)	
Race/ethnicity			< 0.001
Non-Hispanic White	7,143 (49.9)	51,977 (56.2)	
Non-Hispanic Black	1,801 (12.6)	10,694 (11.6)	
Non-Hispanic Asian	1,490 (10.4)	10,541 (11.4)	
Hispanic	3,458 (24.1)	16,649 (18.0)	
Other	435 (3.0)	2,637 (2.8)	
Education			< 0.001
Less than high school	2,288 (16.0)	9,567 (10.3)	
High school	3,565 (24.9)	21,095 (22.8)	
Any postsecondary	8,474 (59.1)	61,856 (66.9)	
Insurance			< 0.001
Medicaid	6,314 (44.1)	34,481 (37.3)	
Private insurance	6,676 (46.6)	52,076 (56.3)	
Self-pay	693 (4.8)	2,853 (3.1)	
Other	644 (4.5)	3,108 (3.3)	
Body mass index, kg/m^2			< 0.001
Underweight (< 18.5)	744 (5.2)	4,542 (4.9)	
Normal (18.5–24.9)	7,318 (51.1)	48,039 (51.9)	
Overweight (25–29.9)	3,633 (25.4)	22,749 (24.6)	
Obese class I (30–34.9)	1,595 (11.1)	10,211 (11.1)	
Obesity class II (35–39.9)	649 (4.5)	4,270 (4.6)	
Obesity class III (≥ 40)	388 (2.7)	2,707 (2.9)	
Prior live births			< 0.001
None	8,028 (56.0)	63,423 (68.6)	
≥ 1	6,299 (44.0)	29,095 (31.4)	
Prior cesarean delivery	711 (5.0)	3,637 (3.9)	
Trimester prenatal care initiated			< 0.001
First	10,789 (75.3)	74,030 (80.0)	
Second	2,596 (18.1)	13,556 (14.6)	
Third	690 (4.8)	4,120 (4.5)	
No prenatal care	252 (1.8)	812 (0.9)	
Preexisting or gestational diabetes	836 (5.8)	6,010 (6.5)	0.003
Gestational hypertension or preeclampsia	680 (4.7)	6,090 (6.6)	< 0.001
Induction of labor	3,443 (24.0)	35,282 (38.1)	< 0.001
Labor augmentation	3,079 (21.5)	33,093 (35.8)	< 0.001
Gestational age at delivery (completed weeks)	39.1±1.2	39.1±1.2	0.057
U.S. census region			< 0.001
North	1,928 (13.4)	15,776 (17.1)	
Midwest	3,436 (24.0)	22,436 (24.2)	
South	4,293 (30.0)	30,824 (33.3)	
West	4,670 (32.6)	23,482 (25.4)	

Data are presented as n (%) except for gestational age where data are presented as mean ± SD.

Reviewer-requested Secondary and Sensitivity Analyses

After excluding neonatal intensive care unit admission and neonatal transfer from our revised composite outcome for neonatal morbidity, the rate of neonatal morbidity was slightly higher among women receiving *versus* not receiving neuraxial analgesia (5,843 [6.3%] *vs.* 785 [5.5%]). Using this revised definition of the composite outcome, the unadjusted risk of neonatal morbidity associated with neuraxial analgesia was 1.15 (95% CI, 1.07 to 1.24; $P < 0.001$). After adjusting for potential confounders, we observed no statistically significant association between neuraxial analgesia and neonatal morbidity (adjusted relative risk, 1.07; 95% CI, 1.00 to 1.16; $P = 0.054$).

Results from models which accounted for within-county clustering using generalized estimating equation models are provided in Supplemental Digital Content 2 (http://links.lww.com/ALN/C490). For our primary outcome, neuraxial anesthesia was associated with an increased risk of neonatal morbidity (adjusted relative risk, 1.18; 95% CI, 1.12 to 1.25; $P < 0.001$). For the revised composite of neonatal morbidity, the adjusted risk was 1.09 (95% CI, 1.02 to 1.17; $P = 0.014$).

Table 2. Unadjusted and Adjusted Associations between Neuraxial Analgesia and Neonatal Morbidity

	Number of Women		Number with Composite Outcome					
	Neuraxial Analgesia	No Neuraxial Analgesia	Neuraxial Analgesia	No Neuraxial Analgesia	Unadjusted Relative Risk (95% CI)	*P* Value	Adjusted Relative Risk (95% CI)*	*P* Value
Operative vaginal deliveries	92,518	14,327	10,409 (11.3%)	1,271 (8.9%)	1.27 (1.20–1.34)	< 0.001	1.19 (1.12–1.26)	< 0.001
Restricted to birthweight < 4000 g	86,262	13,405	9,514 (11.0%)	1,170 (8.7%)	1.26 (1.19–1.34)	< 0.001	1.19 (1.12–1.26)	< 0.001
Stratified analyses								
Forceps	15,863	1,826	1,861 (11.7%)	131 (7.2%)	1.64 (1.38–1.94)	< 0.001	1.50 (1.26–1.78)	< 0.001
Vacuum	76,655	12,501	8,548 (11.2%)	1,140 (9.1%)	1.22 (1.15–1.30)	< 0.001	1.16 (1.09–1.23)	0.009

*Adjusted for maternal age, race, highest educational level, insurance, onset of prenatal care, body mass index, prior live births, prior cesarean, preexisting or gestational diabetes, pregnancy-induced hypertension or preeclampsia, induction of labor, labor augmentation, gestational age, and United States census region.

Table 3. Neonatal Morbidities with and without Neuraxial Analgesia

	No Neuraxial Labor Analgesia (n = 14,327)	Neuraxial Labor Analgesia (n = 92,518)	Adjusted Relative Risk‡ (95% CI)	*P* Value
Neonatal intensive care unit admission*	719 (5.0%)	6,751 (7.3%)	1.36 (1.26–1.46)	< 0.001
Immediate need for assisted ventilation*	584 (4.1%)	4,534 (4.9%)	1.10 (1.01–1.20)	0.027
5-min Apgar score < 7	333 (2.3%)	2,421 (2.6%)	1.07 (0.95–1.20)	0.257
Neonatal transfer to a different facility within 24 h of delivery†	153 (1.1%)	908 (1.0%)	0.93 (0.78–1.10)	0.390
Assisted ventilation > 6 h*	68 (0.5%)	794 (0.9%)	1.60 (1.25–2.05)	< 0.001
Neonatal seizure or serious neurologic dysfunction*	7 (0.1%)	68 (0.1%)	1.46 (0.66–3.21)	0.350

Data presented as n (%).

*Data missing for four patients. †Data missing for five patients. ‡Adjusted for maternal age, race, highest educational level, insurance, onset of prenatal care, body mass index, prior live births, prior cesarean, preexisting or gestational diabetes, pregnancy-induced hypertension or preeclampsia, induction of labor, labor augmentation, gestational age, and United States census region.

Table 4. Unadjusted and Adjusted Risk Differences in Neonatal Morbidity between Women with and without Neuraxial Analgesia

	Unadjusted Risk Difference per 100 Women (95% CI)	*P* Value	Adjusted Risk Difference per 100 Women (95% CI)*	*P* Value
Operative vaginal deliveries	2.4 (1.9–2.9)	< 0.001	1.8 (1.2–2.3)	< 0.001
Restricted to birthweight < 4000 g	2.3 (1.8–2.8)	< 0.001	1.7 (1.1–2.2)	< 0.001
Stratified analyses				
Forceps only (n = 17,686)	4.6 (3.3–5.8)	< 0.001	3.9 (2.5–5.2)	< 0.001
Vacuum only (n = 89,109)	2.0 (1.5–2.6)	< 0.001	1.4 (0.9–2.0)	< 0.001

*Adjusted for maternal age, race, highest educational level, insurance, onset of prenatal care, body mass index, prior live births, prior cesarean, preexisting or gestational diabetes, pregnancy-induced hypertension or preeclampsia, induction of labor, labor augmentation, gestational age, and United States census region.

Details of the propensity score matched cohort and results from the propensity score analysis are provided in the Supplemental Digital Content 3 (http://links.lww.com/ALN/C491) and Supplemental Digital Content 4 (http://links.lww.com/ALN/C492). For our primary outcome, the rate and risk of neonatal morbidity was higher in women receiving *versus* not receiving neuraxial analgesia (10.4% *vs.* 8.9%, respectively; relative risk, 1.18; 95% CI, 1.10 to 1.26; $P < 0.001$). For the revised composite outcome, the association was not statistically different (relative risk, 1.03; 95% CI, 0.93 to 1.23; $P = 0.606$).

Discussion

In this population-based cross-sectional study of 106,845 women who underwent operative vaginal delivery in the United States in 2017, neuraxial analgesia was not associated with a measurable reduction in neonatal morbidity. Contrary to our hypothesis, we observed a small increased risk of neonatal morbidity. After excluding neonatal intensive care admission and neonatal transfer from our composite neonatal outcome, and accounting for clustering by county, this association was either not or marginally statistically significant. Confounding by indication may explain the observed association between neuraxial analgesia and neonatal morbidity. However, this observational administrative dataset, which is unable to measure the clinician decision-making underlying the use of neuraxial analgesia and mode of delivery cannot definitively address this issue. Given these concerns and the small adjusted risk difference of neonatal morbidity associated with neuraxial analgesia, our findings should not be used as justification to advise women against using neuraxial labor analgesia.

Prior research suggests that neuraxial analgesia is not associated with serious neonatal morbidity or acidosis.[25–27] Yet, sparse data exist regarding the potential effects of neuraxial analgesia on neonatal outcomes among women undergoing operative vaginal delivery. In a Cochrane review of analgesia for forceps delivery,[28] only one study (published in 1980) was identified which compared spinal analgesia to a pudendal nerve block; no neonatal morbidity data were reported in this trial. In a more recent single-center study, epidural analgesia was not significantly associated with cephalohematoma among women undergoing forceps delivery (adjusted odds ratio, 0.89 [95% CI, 0.45 to 1.74]) *versus* no epidural analgesia.[6] These wide CI are likely explained by the small number of neonates with cephalohematoma (n = 25). By comparison, our study included other important indicators of neonatal morbidity, including low Apgar scores and neonatal intensive care unit admissions, that are available using national birth certificate data.

Our *a priori* hypothesis was that neuraxial labor analgesia facilitates a controlled, atraumatic operative delivery, thereby resulting in less neonatal morbidity. Our main results indicated no reduction in neonatal morbidity associated with neuraxial analgesia. Instead, in our unadjusted analysis, we observed an increased risk of neonatal morbidity. Although the magnitude of this risk was lower after accounting for potential maternal and obstetric confounders, a small increased risk was observed in our primary multivariable model. Confounding by indication is a possible explanation for these findings. Clinical factors that may influence a decision to use neuraxial labor analgesia, such as prolonged or dystocic labor, immediate or potential fetal compromise, and fetal malposition, may also affect neonatal outcomes. Other potential sources of confounding by indication bias are hospital infrastructure factors. For example, a hospital with an obstetric anesthesia service may be more likely to have a neonatal intensive care unit and, thus, less likely to transfer sick infants to another facility. To address this concern, in *post hoc* analyses, we excluded neonatal intensive care unit and neonatal transfer from our composite of neonatal morbidity and observed no statistically significant association between neuraxial analgesia and the revised composite of neonatal morbidity in our full model and a propensity score matched model. After accounting for clustering by county of birth (the smallest unit of analysis), the adjusted risk for the revised composite outcome was of marginal statistical significance. These findings substantiate why confounding by indication is legitimate concern. Although a randomized trial would limit this and other forms of confounding bias, randomizing women to receive or not receive neuraxial labor analgesia in this context would be inappropriate, unethical, and not feasible. Therefore, prospective studies sourcing clinical data from large delivery hospitals or hospital systems provide the best opportunity to capture data on confounders that are unavailable in administrative or birth certificate datasets.

The observed association between neuraxial analgesia and neonatal outcome could be mediated by a number of obstetric-related factors, including providers' skill and level of experience performing operative vaginal delivery, fetal position and station (the relation between the fetal presenting part and the ischial spines), type of forceps used (*e.g.*, Simpson, Kjelland), suboptimal instrument placement, and method of instrumental delivery (*i.e.*, direct traction forceps *vs.* rotational forceps).[16,29–31] As an example, a rotational forceps delivery may not be tolerated in women experiencing obstructed labor without neuraxial analgesia, but these complex operative vaginal deliveries may be associated with worse neonatal outcomes compared to an uncomplicated vacuum delivery in a patient without neuraxial analgesia. A systematic review of perinatal morbidity after rotational forceps delivery lend support to this assertion.[32] In this review, 8.9% of neonates required neonatal intensive care unit admission and 7.5% experienced neonatal trauma.[32] In our sensitivity analyses, the relative risk of neonatal morbidity associated with neuraxial analgesia varied according to instrument type (forceps, vacuum), with the point estimate of relative risk being slightly higher in the cohort undergoing forceps delivery. Although reasons for these different risk estimates are unclear, the choice of instrument may differ according to the anticipated complexity of delivery. Finally, the presence or absence of neuraxial labor analgesia may influence providers' recommendations for delivery in women with obstructed or prolonged labor. For example, women without a preexisting epidural catheter may be more likely to undergo intrapartum cesarean delivery rather than a difficult operative vaginal delivery without neuraxial analgesia.

Our study has a number of limitations. The major limitation is that the observational nature of our study design means that we cannot determine cause and effect nor whether the decision to perform an operative delivery was made before or

after placement of a neuraxial block. However, in our clinical experience, the practice of initiating neuraxial analgesia specifically for facilitating operative delivery is unusual. Second, nondifferential exposure or outcome misclassification may bias the effect of neuraxial analgesia toward the null.[33] For our exposure, previous studies report high sensitivity (85 to 96%) and a low false discovery rate (14 to 20%) of neuraxial analgesia documentation in birth certificates.[34] By comparison, in a previous study of 103 California hospitals, neonatal intensive care admissions from birth certificate data were underreported (Lin concordance coefficient = 0.33).[35] Studies of national data are lacking on the accuracy of neonatal complications reported on the birth certificate. Third, drug data are not recorded on the birth certificate, therefore we could not assess the effect of neuraxial drug type or dose on the reported association. Although older studies using high-concentration local anesthetic solutions to induce and maintain neuraxial analgesia found an association between neuraxial labor analgesia and operative vaginal delivery, recent investigations of low-concentration solutions used in contemporary practice have not.[26,36] In addition, details were not available for other analgesic modalities, including systemic opioids or nitrous oxide analgesia, which may have been used by women in the nonneuraxial group.

Based on the findings of this national cohort of women who underwent operative vaginal delivery in 2017, a neonatal benefit of neuraxial analgesia for operative vaginal delivery was not observed. Confounding by indication may explain the observed association between neuraxial analgesia and neonatal morbidity.

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Competing Interests

The authors declare no competing interests.

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