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A Systematic Review and Meta-analysis of Clinical Trials of Neuraxial, Intravenous, and Inhalational Anesthesia for External Cephalic Version

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BACKGROUND: External cephalic version (ECV) is a frequently performed obstetric procedure for fetal breech presentation to avoid cesarean delivery. Neuraxial, intravenous, and inhalational anesthetic techniques have been studied to reduce maternal discomfort caused by the forceful manipulation. This study compares the effects of these anesthetic techniques on ECV and incidence of cesarean delivery.

METHODS: We conducted a comprehensive literature search for published randomized controlled trials (RCTs) or well-conducted quasi-randomized trials of ECV performed either without anesthesia or under neuraxial, intravenous, or inhalational anesthesia. Pairwise random-effects meta-analyses and network meta-analyses were performed to compare and rank the perinatal outcomes of the 3 anesthetic interventions and no anesthesia control, including the rate of successful version, cesarean delivery, maternal hypotension, nonreassuring fetal response, and adequacy of maternal pain control/satisfaction.

RESULTS: Eighteen RCTs and 1 quasi-randomized trial involving a total of 2296 term parturients with a noncephalic presenting singleton fetus were included. ECV under neuraxial anesthesia had significantly higher odds of successful fetal version compared to control (odds ratio [OR] = 2.59; 95% confidence interval [CI], 1.88–3.57), compared to intravenous anesthesia (OR = 2.08; 95% CI, 1.36–3.16), and compared to inhalational anesthesia (OR = 2.30; 95% CI, 1.33–4.00). No association was found between anesthesia interventions and rate of cesarean delivery. Neuraxial anesthesia was associated with higher odds of maternal hypotension (OR = 9.33; 95% CI, 3.14–27.68). Intravenous anesthesia was associated with significantly lower odds of nonreassuring fetal response compared to control (OR = 0.36; 95% CI, 0.16–0.82). Patients received neuraxial anesthesia reported significantly lower visual analog scale (VAS) of procedure-related pain (standardized mean difference [SMD] = −1.61; 95% CI, −1.92 to −1.31). The VAS scores of pain were also significantly lower with intravenous (SMD = −1.61; 95% CI, −1.92 to −1.31) and inhalational (SMD = −1.19; 95% CI, −1.58 to −0.8) anesthesia. The VAS of patient satisfaction was significantly higher with intravenous anesthesia (SMD = 1.53; 95% CI, 0.64–2.43).

CONCLUSIONS: Compared to control, ECV with neuraxial anesthesia had a significantly higher successful rate; however, the odds of maternal hypotension increased significantly. All anesthesia interventions provided significant reduction of procedure-related pain. Intravenous anesthesia had significantly higher score in patient satisfaction and lower odds of nonreassuring fetal response. No evidence indicated that anesthesia interventions were associated with significant decrease in the incidence of cesarean delivery compared to control. (Anesth Analg 2020;131:1800–11)

KEY POINTS

- **Questions:** Can anesthesia intervention facilitate successful external cephalic version (ECV) and decrease incidence of cesarean delivery?
- **Findings:** ECV with neuraxial anesthesia had a significantly higher procedure success rate; however, neither the involvement of neuraxial, intravenous, nor inhalational anesthesia significantly reduced the incidence of cesarean delivery.
- **Meaning:** The decision of managing ECV with or without certain types of anesthesia intervention should be made on an individual basis.

GLOSSARY

ACOG = American College of Obstetricians and Gynecologists; **CI** = confidence interval; **ECV** = external cephalic version; **GRADE** = Grading of Recommendations Assessment, Development and Evaluation; **inhal** = inhalational; **iv** = intravenous; **OR** = odds ratio; **PO** = by mouth; **PRISMA** = Preferred Reporting Items for Systemic Reviews and Meta-analysis; **RCT** = randomized controlled trial; **REML** = restricted maximum likelihood; **SMD** = standardized mean difference; **SOAP** = Society for Obstetric Anesthesia and Perinatology; **SQ** = subcutaneous; **SUCRA** = surface under the cumulative ranking curve; **VAS** = visual analog scale

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External cephalic version (ECV) is an effective obstetrical procedure to facilitate vaginal delivery for term parturient with noncephalic fetal presentations. Data from multiple studies and a recent meta-analysis indicate that successful ECV at term significantly reduces the rate of cesarean delivery and the overall cost of care.[1–3] There were no significantly increased perinatal complications in parturients who received ECV.[4,5] Based on strong available evidence, the American College of Obstetricians and Gynecologists (ACOG) recommended that all women who are near term with breech presentations should be offered an ECV attempt if there are no contraindications.

Several interventions, including application of tocolytic agents, anesthetic managements, and more adjuvant interventions,[6–8] have been investigated extensively aiming at increasing rate of successful ECV and improving overall perinatal outcomes. While tocolysis has been proven to be effective for facilitating ECV, the involvement of anesthesia care in ECV is not without controversy.[9] Early studies indicated that the involvement of general anesthesia was associated with higher incidence of maternal and fetal complications.[10] Studies with neuraxial anesthesia showed mixed results of ECV success and the incidence of cesarean delivery.[11–13] More recently, inhalational and intravenous anesthesia have been re-evaluated in ECV as well. Currently, there is no consensus guideline from ACOG or the Society for Obstetric Anesthesia and Perinatology (SOAP) regarding if and how anesthesia care should be managed in ECV.

The current study was designed to synthesize available data from the published randomized controlled trials (RCTs) and well-conducted quasi-RCTs and compare the maternal and fetal outcomes of ECV without and with neuraxial, inhalational, and intravenous anesthesia through pairwise and network meta-analysis. The goal is to compare the effects of these anesthetic techniques on ECV and incidence of cesarean delivery.

METHODS

Literature Search Strategies and Data Extraction

This systematic review and meta-analysis were conducted based on criteria of the Preferred Reporting Items for Systemic Reviews and Meta-analysis (PRISMA) statement.[14] The registration number with PROSPERO is CRD42018110100. We systematically searched Ovid Medline, Cochrane CENTRAL, PubMed, EMBASE, CINAHL, and Google Scholars for RCTs or well-conducted trials that studied success rates and other relevant maternal and fetal outcomes of ECV with or without assistance of neuraxial, intravenous, or inhalational anesthesia. Search terms included breech presentation, external cephalic version, neuraxial anesthesia, epidural anesthesia, spinal anesthesia, inhalational anesthesia, intravenous anesthesia, and so on (see Supplemental Digital Content, Appendix 1, http://links.lww.com/AA/D69, for database search strategy for Ovid Medline). We also manually searched for studies listed in the references of enrolled articles in case there were potential studies not captured by the database search strategy. There is no limitation on language.

We included original full-text articles or meeting abstracts that (1) were RCTs published in peer-reviewed journals from 1946 (the earliest year that publications are searchable in the online databases) to May 2019; (2) compared ECV with and without assistance of neuraxial, intravenous, or inhalational anesthesia; and (3) assessed outcomes including procedure success rates, incidence of cesarean delivery, pain associated with ECV, patient satisfaction rate, maternal hypotension, and/or nonreassuring fetal response. If there were several studies based on the same cohort, the studies with the most recent and relevant results were enrolled.

Study selection was conducted in these steps: 2 reviewers (Q.H. and S.R.) worked independently to screen titles along with abstracts retrieved by literature searches conducted according to the predefined search protocols. The disagreements were resolved by joint reviewing of 3 investigators (X.Z., L.Z., and X.W.). Full-text studies and published abstracts that met the above inclusion criteria were enrolled for final systematic review and meta-analyses. Two reviewers (Q.H. and S.R.) independently collected relevant data from each enrolled study using a predesigned Excel data form. The collected data, which included characteristics of each studies, patient baseline information, study design, procedural details, and ECV-related maternal and fetal outcomes, were verified,

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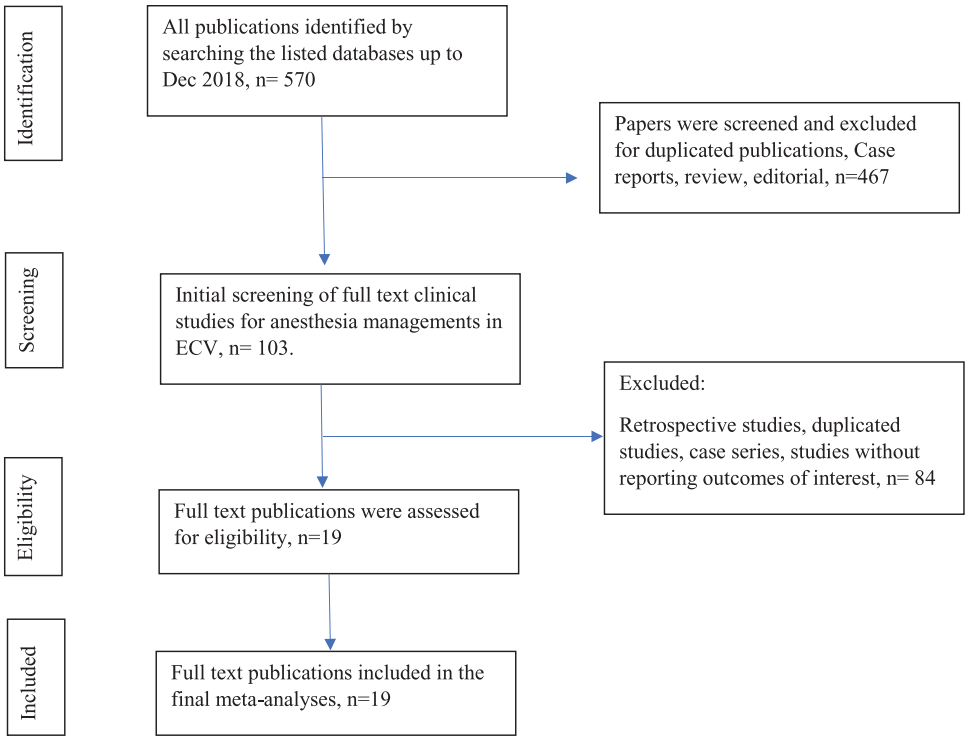

Figure 1. Flow chart for literature enrollment from identification to final synthesis according to the PRISMA protocol. ECV indicates external cephalic version; PRISMA, Preferred Reporting Items for Systemic Reviews and Meta-analysis.

and disagreements were resolved by joint reviewing of 3 reviewers (X.Z., L.Z., and X.W.). Figure 1 summarizes the complete process of paper study enrollment according to the PRISMA statement.

Quality Assessment

The included studies were evaluated by 2 reviewers using the Cochrane risk of bias assessment tool,[32] which evaluated 6 domains including random assignment, allocation concealment, blinding of participants, incomplete outcome data, selective outcome reporting, and other sources of bias. The assessment of "high," "low," or "unclear" was assigned to each domain for respective designation of a risk of bias. If unclear was assigned to ≤1 domain, the study was evaluated as having a low risk of bias; if 2 or 3 domains were assigned unclear, the study was evaluated as having moderate risk of bias; and if >3 domains were assigned unclear, the study was evaluated as having a high risk.[33] To determine confidence in each estimate of effect size from a network meta-analysis, we follow the standard Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group for pairwise meta-analyses.[34]

Statistical Analyses

Network meta-analysis was performed to incorporate multiple comparisons for each available outcome using multivariable meta-analyses under the frequentist framework,[35] where the within-network heterogeneity was assumed common and the heterogeneity variance was estimated using restricted maximum likelihood (REML). For multiarmed studies, side-splitting model was used to estimate parameters for both sides.[36] Direct evidence on effect sizes was reported from pairwise meta-analysis using random-effects model, when limited studies existed to estimate the indirect comparison (ie, ≥3 studies for adjacent edges with common comparison treatment in a closed loop). Zero cells were adjusted using Haldane–Anscombe correction.[37,38] Odds ratios (ORs) and 95% confidence intervals (95% CIs) were estimated for binary outcomes. Standardized mean differences (SMDs) and 95% CIs were calculated for continuous outcomes. The pooled OR is considered statistically significant if 95% CI did not contain 1, and the pooled SMD is considered statistically significant if 95% CI did not contain 0. Individual and pooled estimates were illustrated using forest plots. For any closed triangle loop among 3 anesthesia comparisons (where ≥2 studies were reported for each of the pairwise comparison), the direct and indirect comparisons were integrated to evaluate the effect sizes (ORs, SMDs) and 95% CIs. For open triangle loop among 3 anesthesia comparisons (if any pairwise comparison had <2 studies), direct estimates from pairwise meta-analysis were reported including ORs, SMDs, and 95% CIs. Global tests for

inconsistency were performed using the Wald test statistic, which follows a χ^2 distribution under the consistency assumption. P value >.05 indicates no evidence of inconsistency. The cumulative rankings of treatment effect sizes were computed to identify superiority.[39] Publication bias was evaluated using funnel plots. Sensitivity analysis was conducted by excluding studies that were considered to have different designs (or anesthesia interventions) compared to other enrolled studies. All analyses were conducted using Stata 14 (Stata Corp, College Station, TX).

RESULTS

Study Characteristics

A total of 2296 patients were recorded in the 19 included studies. Sixteen RCTs and 1 quasi-randomized trial belonged to a 2-arm trial, and 2 were in the category of a 3-arm trial. The Table summarizes the study characteristics including the study regions, gestational ages, samples sizes, operators and version attempts, primary outcomes, managements of tocolyses, and anesthesia interventions. Supplemental Digital Content, Table S1, http://links.lww.com/AA/D69, lists all the sample sizes used for the calculation of the odds ratios in the pairwise or network meta-analyses.

Quality Assessment

Two reviewers independently assessed concealment of allocation, blinding, and adequacy of analyses. To represent the overall quality, all enrolled studies were evaluated according to the Cochrane risk of bias assessment tool. Note that risk of bias can differ across different outcomes of interest, as each outcome draws from a different subset of studies for the meta-analysis. Following adapted GRADE approach,[40] the contributions of all direct estimates from the contribution matrix were integrated to the risk of bias judgment for each of the pairwise network estimate. In the bar chart, we conventionally used green, yellow, and red to represent low, moderate, and high risk of bias for each of the pairwise comparisons in the network meta-analysis. To ensure that the relative contributions of different sources of direct evidence are accounted for appropriately, we presented risk of bias for each network estimate that integrated pairwise comparisons for successful fetal version and cesarean delivery (see Supplemental Digital Content, Appendix 2, http://links.lww.com/AA/D69).

Meta-analysis and Network Meta-analysis

Successful Fetal Version (Network Meta-analysis). There were 10 studies comparing neuraxial anesthesia versus control, 2 studies inhalational anesthesia versus control, 4 studies intravenous anesthesia versus control, and 2 multiarm studies among intravenous anesthesia, neuraxial anesthesia, and control (see network geometry plot in Figure 2). The global test for inconsistency suggested no presence of inconsistency (χ^2 statistic = 8.37; P = .08). Network ranking of cumulative probability indicated that neuraxial anesthesia was the best treatment with the largest surface under the cumulative ranking curve (SUCRA) of successful fetal version (see SUCRA plot in Figure 2). The larger the SUCRA is, the better the treatment in increasing the successful fetal version rate. Patients receiving neuraxial anesthesia had significantly higher events in successful fetal version when compared to control (OR = 2.59; 95% CI, 1.88–3.57); compared to intravenous anesthesia (OR = 2.08; 95% CI, 1.36–3.16); and compared to inhalational anesthesia (OR = 2.30; 95% CI, 1.33–4.00). Network meta-analysis indicated that the rate of successful version between either intravenous or inhalational anesthesia and control was comparable. Funnel plot for all pairwise comparisons was presented, which indicated no publication bias (see Supplemental Digital Content, Appendix 3, Figure S3.1, http://links.lww.com/AA/D69).

Cesarean Delivery (Network Meta-analysis). There were 6 studies comparing neuraxial anesthesia versus control, 3 studies comparing intravenous anesthesia versus control, 2 studies comparing neuraxial anesthesia versus intravenous anesthesia, and one multiarm study comparing among intravenous anesthesia, neuraxial anesthesia, and control (see network geometry plot in Figure 3). The global test for inconsistency suggested no presence of inconsistency (χ^2 statistic = 3.39; P = .34). Network meta-analysis results did not reveal significant differences in the odds of cesarean delivery among all management groups and control, which is consistent with SUCRA plot (Figure 3). Funnel plot for all pairwise comparisons implied that potential publication bias existed between neuraxial anesthesia and control (see Supplemental Digital Content, Appendix 3, Figure S3.2, http://links.lww.com/AA/D69).

Emergent Cesarean Delivery (Meta-analysis). There were 3 studies comparing neuraxial anesthesia versus control, 2 studies comparing neuraxial versus intravenous anesthesia, and 1 study each for inhalational anesthesia versus control and neuraxial anesthesia versus control. Because there is not enough direct evidence to conduct network meta-analysis, meta-analysis with random effects was performed for pairwise comparisons containing >2 studies. Forest plot for pairwise comparisons showed that neuraxial anesthesia was associated with a 2.47-fold increase of emergent cesarean delivery compared to control, while the association was insignificant because the CI covered 1 (OR = 2.47; 95%

Table. Baseline Characteristics of Enrolled Clinical Trials

Studies	Region	Gestational Age		Sample Size				No. ECV Operators	ECV Attempts	Primary Outcomes	Tocolysis	Dosage of Anesthesia				
		Intervention	Control	Neuraxial	IV	Inhalational	Control					Intrathecal	Epidural	IV	Inhalational	Control
Schorr et al,[15] 1997	United States	38.0 ± 2.3	37.4 ± 2.1	35			34	Not specified	3	Successful ECV	SQ terbutaline 0.25 mg, 30-min interval		2% lidocaine titrate to T6 level			
Dugoff et al,[13] 1999	United States	38.0 ± 0.2	38.0 ± 0.2	50			52	2	4	Successful ECV	IV terbutaline 0.25 mg	0.25% bupivacaine 1 mL, 10 µg Sufentanil				
Mancuso et al,[16] 2000	United States	38.1 ± 1.2	37.9 ± 1.0	54			54	Not specified	No limit	Successful ECV	SQ terbutaline 0.25 mg		2% lidocaine 13 mL with fentanyl 100 µg			
Birnbach et al,[17] 2001	United States	37.0 ± 0.7	36.9 ± 0.4	20			15	Not specified	Not specified	Successful ECV	SQ terbutaline 0.25 mg	IV sufentanil 10 µg		IV meperidine 50 mg		
Delisle et al,[18] 2001	Canada	>36	>36	73			68	Not specified	4	Successful ECV	IV nitroglycerine dose not specified	Intrathecal 0.25% bupivacaine 1 mL with fentanyl 20 µg				
Hollard et al,[19] 2003	United States	>36	>36	17			19	Not specified	Not specified	Successful ECV, pain	SQ terbutaline 0.25 mg	Lidocaine 6 mg, fentanyl 15 µg				
Weiniger et a l,[20] 2007	Israel	37.9 ± 1.0	37.9 ± 1.0	36			34	Not specified	3	Successful ECV	IV ritodrine 50 mg, PO nifedipine 20 mg after 2003	7.5 mg bupivacaine				
Leung et al,[21] 2009	China	Not specified	Not specified	40	40		40	Not specified	Not specified	Success rate of ECV, pain	Hexoprenaline, dose not specified	Not specified		Not specified		
Sullivan et al,[22] 2009	United States	>36	>36	47	48			Not specified	Not specified	Successful ECV	IV terbutaline 0.25 mg	Intrathecal bupivacaine 2.5 mg with fentanyl 15 µg; epidural lidocaine 45 mg with epinephrine 15 µg	Lidocaine 45 mg, fentanyl 15 µg	IV 50 µg fentanyl		
Weiniger et al,[11] 2010	Israel	38.1 ± 0.9	38.2 ± 1.1	31			33	Not specified	Not specified	Successful ECV	IV ritodrine 50 mg, PO nifedipine 20 mg after 2003	Bupivacaine 7.5 mg				

(Continued)

Table. Continued

Studies	Region	Gestational Age		Sample Size				No. ECV Operators	ECV Attempts	Primary Outcomes	Tocolysis	Dosage of Anesthesia				
		Intervention	Control	Neuraxial	IV	Inhalational	Control					Intrathecal	Epidural	IV	Inhalational	Control
Burgos et al,[23] 2013	Spain	>37	>37			300	150	3	5	Successful ECV	IV ritodrine 200 µg/min for 30 min, or atosiban 6.75 mg				50% nitrous oxide for 3 min	
Muñoz et al,[24] 2014	Spain	36–41	36–41		31		29	Not specified	Not specified	Pain associated with ECV	IV infusion ritodrine 200 µg/min continuously			Remifentanil 0.1 µg/kg/min infusion, 0.1 µg/kg on demand		Paracetamol 1 g
Pinel Perez et al,[25] 2015	Spain	Not specified	Not specified	44		57		Not specified	Not specified	Success rate of ECV	Not specified	Not specified			4% sevoflurane	
Khaw et al,[26] 2015	China	36.9	37.3	63	63		63	5	5	Successful ECV	Hexoprenaline 10 µg	0.5% bupivacaine 1.8 mL with fentanyl 15 µg		Remifentanil 0.1 µg/kg/min infusion		
Liu and Xue,[27] 2016	China	37–41	37–40		76		76	Not specified	Not specified	Successful ECV	Not specified			Remifentanil 0.1 µg/kg/min for 3 min, 0.1 µg/kg on demand		Paracetamol 1 g
Li et al,[28] 2016	China	36.0 ± 2.7	35. ± 1.9	60			30	Not specified	Not specified	Successful ECV	Not specified	1.73% lidocaine 10 mL or 3 mL with intrathecal bupivacaine 2.5 mg				
Burgos et al, [29] 2016	Spain	37–41	37–40		60	60				Successful ECV	IV ritodrine 200 µg/min for 30 min, or atosiban 6.75 mg			Remifentanil 0.1 µg/kg/min × 3 min, 0.1 µg/kg on demand	50% nitrous oxide for 3 min	
Wang et al,[30] 2017	China	37–41	37–41		72		72	Not specified	Not specified	Pain associated with ECV	Not specified			Remifentanil 0.1 µg/kg/min for 3 min, 0.1 µg/kg on demand		Paracetamol 1 g
Dochez et al,[31] 2017	France	Not specified	Not specified			74	76			Successful ECV, pain	Not specified				50% nitrous oxide	Medical air

Abbreviations: ECV, external cephalic version; IV, intravenous; PO, by mouth; SQ, subcutaneous.

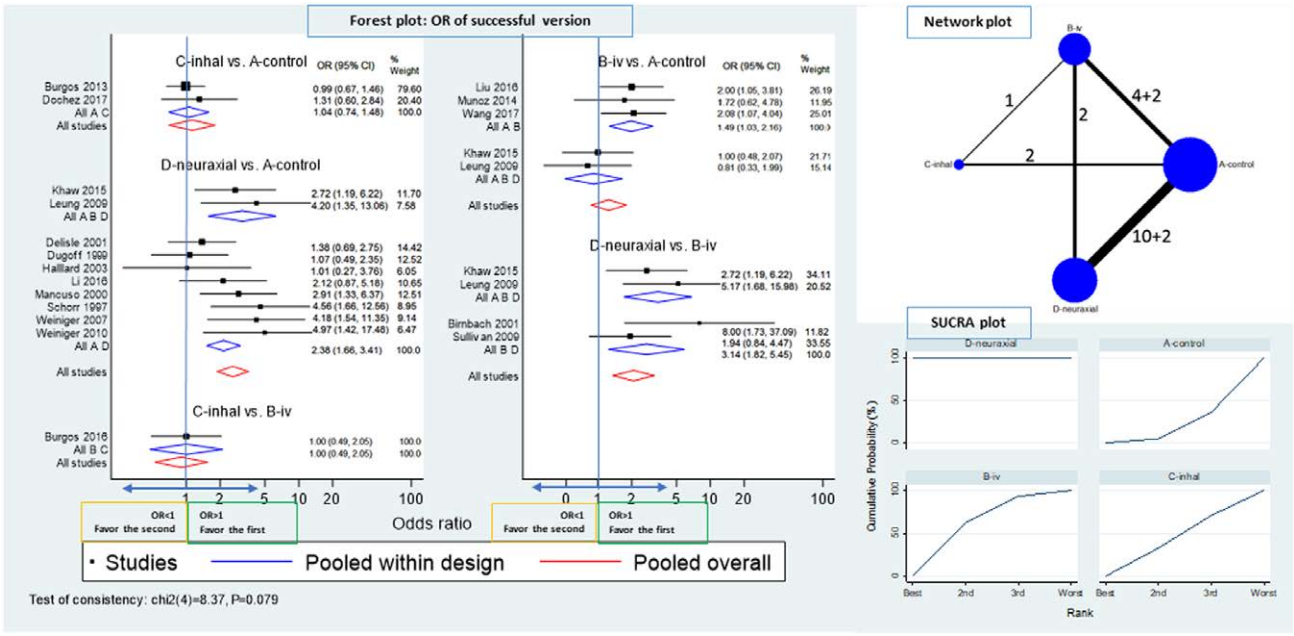

Figure 2. Network meta-analysis results for successful fetal version. Neuraxial anesthesia is associated with significantly higher odds of successful version. Forest plot: OR >1 indicated that the first treatment in pairwise comparison is associated with higher odds of successful version; thus, the first treatment was favored compared to the second. Network plot: 10 studies comparing neuraxial anesthesia versus control, 2 studies inhal anesthesia versus control, 4 studies iv anesthesia versus control, and 2 multiarm studies among iv anesthesia, neuraxial anesthesia, and control. SUCRA plot: The treatments were ranked by the SUCRA. The larger the SUCRA, the better the treatment in increasing the successful version rates. The rank in successful version is D, neuraxial > B, iv > A, control > C, inhal anesthesia. CI indicates confidence interval; inhal, inhalational; iv, intravenous; OR, odds ratio; SUCRA, surface under the cumulative ranking curve.

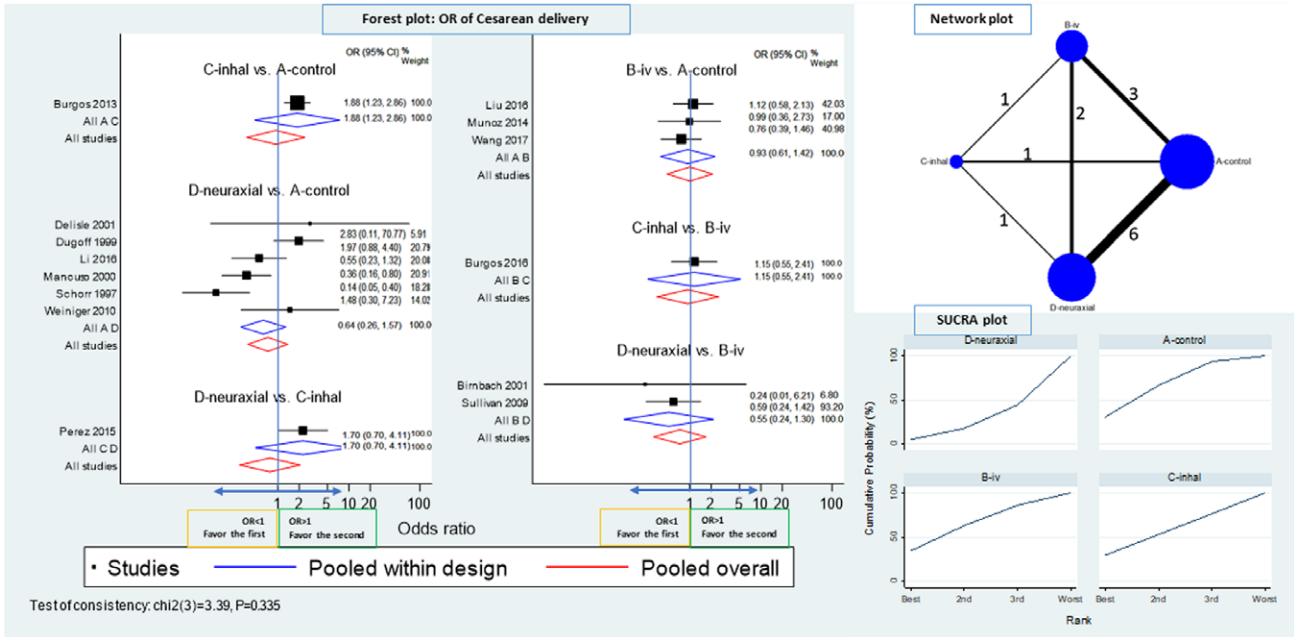

Figure 3. Network meta-analysis results for cesarean delivery. The rankings in cesarean delivery were relatively comparable. Forest plot: OR <1 indicated that the first treatment in pairwise comparison is associated with lower odds of cesarean delivery; thus, the first treatment was favored compared to the second. Network plot: 6 studies comparing neuraxial anesthesia versus control, 3 studies inhal versus control, 2 studies neuraxial versus iv anesthesia, and one multiarm study among iv anesthesia, neuraxial anesthesia, and control. SUCRA plot: The treatments were ranked by the SUCRA. The smaller the SUCRA, the better the treatment in decreasing cesarean delivery rates. CI indicates confidence interval; inhal, inhalational; iv, intravenous; OR, odds ratio; SUCRA, surface under the cumulative ranking curve.

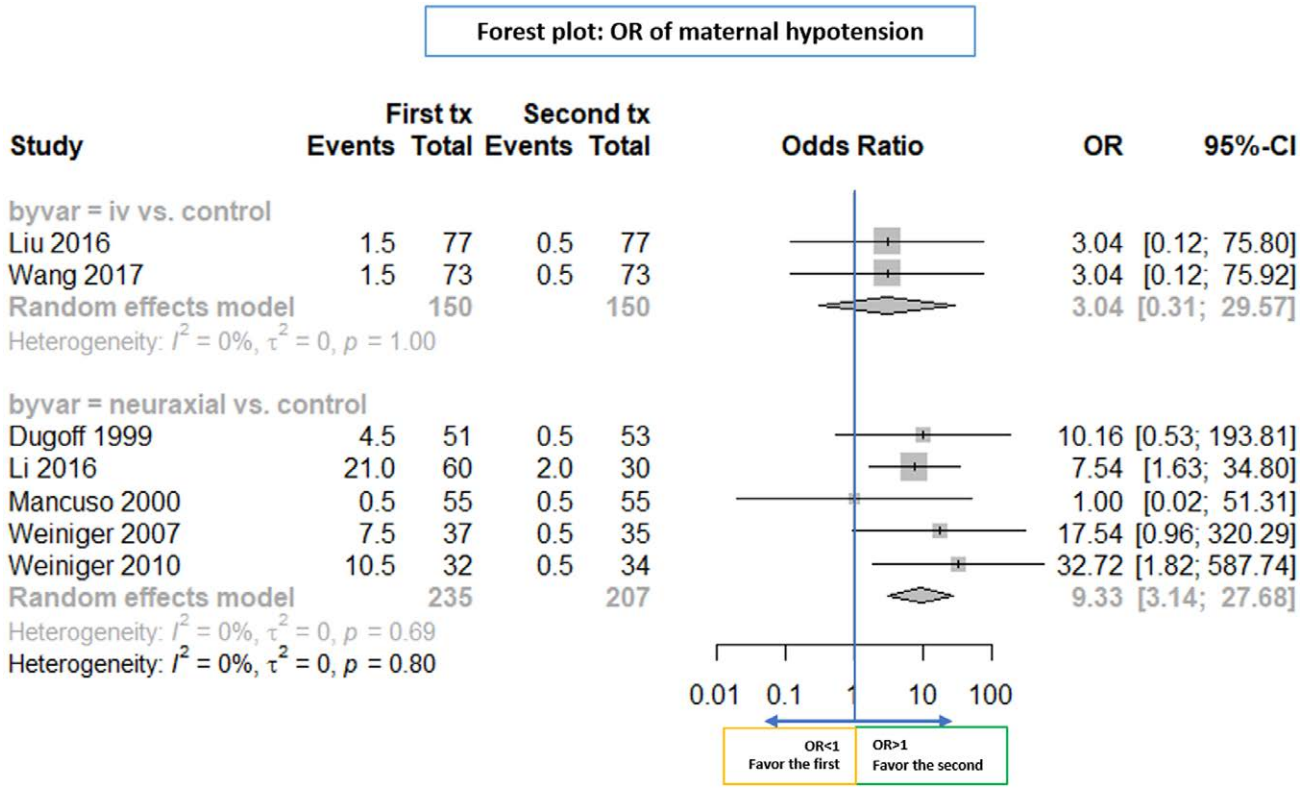

Figure 4. Forest plot of maternal hypotension with pairwise comparison from meta-analysis. Neuraxial anesthesia is associated with significantly higher odds of maternal hypotension. CI indicates confidence interval; OR, odds ratio.

CI, 0.61–10.05). There was no heterogeneity (I^2 = 0%; P = .67). Note here for pairwise comparisons in funnel plot, there were not enough studies to properly evaluate the evidence of publication bias (see Supplemental Digital Content, Appendix 4, Figure S4.1, Figure S4.2, http://links.lww.com/AA/D69).

Maternal Hypotension (Meta-analysis). There were 5 studies comparing neuraxial anesthesia versus control, 3 studies intravenous anesthesia versus control, and one study each for inhalational anesthesia versus control, inhalational versus intravenous anesthesia, and intravenous versus neuraxial anesthesia. Because there is not enough direct evidence to conduct network meta-analysis, meta-analysis with random effects was performed for pairwise comparisons containing >2 studies. The forest plot for pairwise comparisons (Figure 4) showed that neuraxial anesthesia was associated with higher odds of maternal hypotension than control (OR = 9.33; 95% CI, 3.14–27.68), with little to no evidence of heterogeneity (I^2 = 0%, P = .69). The funnel plot for the pairwise comparison indicated no publication bias for neuraxial anesthesia versus control. Note here for pairwise comparisons of intravenous anesthesia versus control, there were not enough studies to properly evaluate the evidence of publication bias (see Supplemental Digital Content, Appendix 3, Figure S3.3, http://links.lww.com/AA/D69).

Nonreassuring Fetal Response (Meta-analysis). There were 6 studies comparing neuraxial anesthesia versus control, 3 studies comparing intravenous anesthesia versus control, and 1 study comparing inhalational anesthesia versus control on the fetal heart rate response. Because there is not enough direct evidence to conduct network meta-analysis, pairwise meta-analysis with random effects was performed for pairwise comparisons containing ≥2 studies. Forest plot for pairwise comparisons (Figure 5) indicated that intravenous anesthesia was associated with lower odds in nonreassuring fetal response compared to control (OR = 0.36; 95% CI, 0.16–0.82) with little to no evidence of heterogeneity (I^2 = 0%; P = .79). There was not enough evidence indicated that neuraxial anesthesia was associated with nonreassuring fetal response (OR = 2.45; 95% CI, 0.94–6.34). Funnel plot for the pairwise comparison did not indicate obvious publication bias (see Supplemental Digital Content, Appendix 3, Figure S3.4, http://links.lww.com/AA/D69).

Visual Analog Scale Pain and Satisfaction (Meta-analysis). There were 3 studies comparing neuraxial anesthesia versus control, 4 studies comparing intravenous anesthesia versus control, and one study comparing inhalational versus intravenous anesthesia on the outcome of procedure-related pain. Because there is not enough direct evidence to conduct network meta-analysis, pairwise meta-analysis with random effects

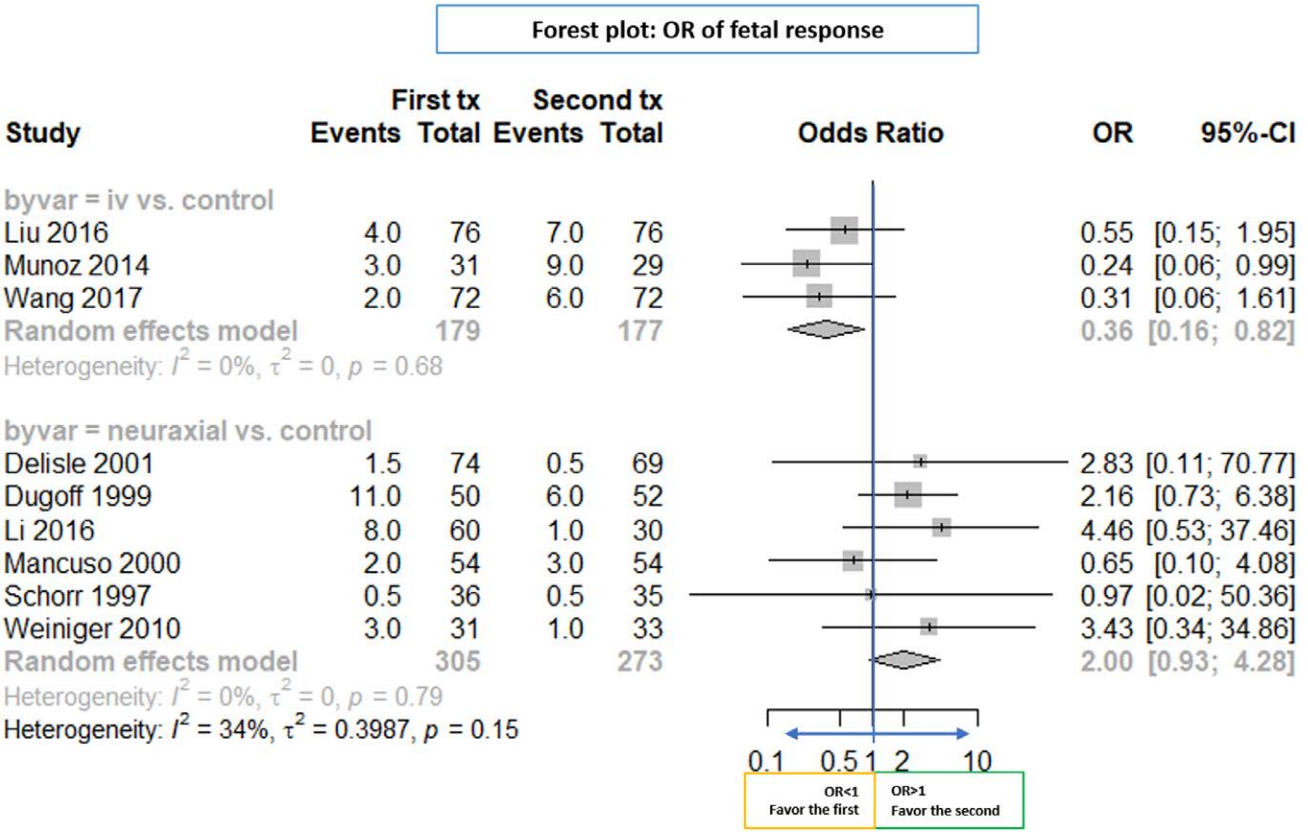

Figure 5. Forest plot of nonreassuring fetal response with pairwise comparison from meta-analysis. Intravenous anesthesia is associated with lower odds of nonreassuring fetal response. CI indicates confidence interval; OR, odds ratio.

was performed for pairwise comparisons containing ≥2 studies. Forest plot for pairwise comparisons (see Supplemental Digital Content, Appendix 5, Figure S5.1, http://links.lww.com/AA/D69) showed that patients receiving neuraxial or intravenous anesthesia reported a significantly lower visual analog scale (VAS) of procedure-related pain (SMD = −1.61; 95% CI, −1.92 to −1.31) with little to no evidence of heterogeneity (I^2 = 0%; P = .70) compared to control. When compared to control, VAS of procedure-related pain tended to be lower but with high heterogeneity in intravenous anesthesia (SMD = −1.35; 95% CI, −2.45 to −0.25; I^2 = 96%; P < .001). There was no significant difference in VAS of satisfaction between parturients received no anesthesia and those had intravenous anesthesia (SMD = 1.53; 95% CI, 0.64–2.43). Parturients were more satisfied with inhalational anesthesia; however, the data were not enough for synthesis. Note here for pairwise comparisons of intravenous anesthesia versus control, there were not enough studies to properly evaluate the evidence of publication bias (see Supplemental Digital Content, Appendix 5, Figure S5.2, http://links.lww.com/AA/D69).

Sensitivity Analysis

To evaluate how robust the above results from meta-analysis, we performed sensitivity analysis by excluding Burgos et al[23] (2013; due to the study design) and Pinel Perez et al[25] (2015; due to the heterogeneous inhaled anesthesia), respectively. The results remained consistent with the main analysis results as presented above.

To further define the potential association between the anesthetic interventions and cesarean delivery, we conducted additional sensitivity analysis excluding the studies which allow breech trial and/or rescue ECV after the failure of the initial procedures. The global test for inconsistency suggested no presence of inconsistency (χ^2 statistic = 0.09; P = .76). Network meta-analysis results did not reveal significant differences in the odds of cesarean delivery among all management groups and control, which is consistent with cumulative ranking (Supplemental Digital Content, Figure S6, http://links.lww.com/AA/D69).

DISCUSSION

To summarize the findings of our study, all anesthesia techniques provide maternal pain relief during ECV. Neuraxial anesthesia was associated with significantly increased ECV success rate, although there was no significant difference in the incidence of cesarean delivery among any of the groups, including the group with no anesthesia control. Neuraxial

anesthesia was associated with higher odds of maternal hypotension, but other outcomes were not different from other groups, including nonreassuring fetal response and emergent cesarean. Intravenous anesthesia was associated with significantly lower odds of nonreassuring fetal response and higher maternal satisfaction than any of the other groups.

Data from early studies discouraged performing ECV under general anesthesia due to high incidence of maternal and fetal complications.[10,41] Recent meta-analysis suggested that neuraxial anesthesia had significant benefits of pain relief, facilitating fetal version and decrease incidence of cesarean delivery.[42] However, a survey of SOAP members found that majority of the respondents never or rarely apply neuraxial anesthesia in ECV.[43] Currently, ACOG and SOAP do not have a consensus guideline for anesthesia management in ECV.[44] We feel that a comprehensive evaluation of the risks and benefits of the neuraxial, intravenous, and inhalational anesthesia interventions in ECV is necessary.

Our results indicate that all anesthesia techniques reduced maternal pain associated with ECV, with neuraxial anesthesia being the most effective. Noticeably, good pain relief by neuraxial anesthesia was not necessarily associated with higher patient satisfaction. The parturient seemed to be more satisfied with intravenous and inhalational anesthesia, which may be related to the procedure discomfort or complications from neuraxial anesthesia; the convenience and comfort of delivering intravenous and inhalational agents reduced barriers to acceptance. In addition, there is no consensus of the appropriate dosage of local or, in the case of intravenous and inhalational anesthesia, systemic anesthetics for providing adequate pain relief, abdominal wall relaxation, and minimizing the risk of complications. A recent study of ECV with spinal anesthesia revealed that as little as one-third of the dose of surgical anesthesia was adequate to facilitate successful ECV.[45] More studies of the dose–response for neuraxial and systemic anesthesia interventions are warranted.

Past studies indicated that successful ECV was associated with decreased rate of cesarean delivery, although the parturients with successful ECV had higher incidence of cesarean delivery compared to normal controls.[46] In the current study, neuraxial anesthesia, but not intravenous anesthesia or inhalational anesthesia, was associated with significantly increased success rate of ECV; however, none of the anesthesia interventions were associated with significantly decreased incidence of cesarean delivery. This result is different from that of Magro-Malosso et al,[42] which indicated significantly reduced incidence of cesarean delivery. The discrepancy may be explained by the differences of study inclusion, method for meta-analysis, and data processing. Our data suggest that the benefit of reducing overall incidence of cesarean delivery from successful ECV under neuraxial anesthesia might be negated by the potential increased risk of emergent cesarean delivery. However, this remains inconclusive due to the limitation of enrolled studies.

Fetal distress is the most important indication for emergent cesarean. Our data indicated that neuraxial anesthesia was associated with significantly higher odds of maternal hypotension, suggesting that maternal hemodynamic instability associated with neuraxial anesthesia may be a risk of fetal distress from ECV. Maternal hypotension is a common preventable complication of neuraxial anesthesia; the maintaining of maternal hemodynamic stability is pivotal for improving the perinatal outcomes.[47–50] It is reasonable to postulate that proactively preventing and treating maternal hypotension during ECV may help reduce the risk of emergent cesarean. Further clinical studies are needed to define the association between hemodynamic control and the incidence of emergent cesarean during ECV under neuraxial or systemic anesthesia.

We have no doubt that successful ECV with favorable maternal and fetal outcomes depends on the experience and hands-on skills of the obstetricians. Naturally, maternal discomfort related guarding of maternal abdominal and uterine muscles is protective for the fetus. The application of tocolytic agents and neuraxial or systemic anesthetics may produce the desirable effects of abdominal wall and uterine relaxation, which make turning the fetus easier[51,52]; however, the unchanged odds of cesarean delivery despite the significantly increased rates of successful ECV indicated that there may be confounding factors responsible for increased incidence of urgent or emergent cesarean delivery. We suspect that the relaxation of abdominal wall and uterine muscles may render the uterus and fetus vulnerable to injuries caused by external turning maneuvers. This is an important issue to investigate in future clinical studies. We believe that the key to achieve better perinatal outcomes associated with ECV is the combination of good experience and procedural skills of obstetricians and appropriately managed neuraxial or systemic anesthesia intervention. There is no single best anesthesia technique, the decision to proceed with or without anesthesia intervention should be made jointly by the parturient, her obstetrician, and the anesthesiologist on the individual basis.

The current systemic review and network meta-analysis has several limitations: (1) the insufficient number of studies does not allow us to separately compare different types of neuraxial and inhalational anesthesia because the available data are not enough

to perform network meta-analysis for evaluating individual type of anesthetic technique; (2) most of the enrolled RCTs have small sample size, which could increase the risk of selection bias; (3) all trials were designed for investigating successful ECV as primary outcome and are underpowered for detecting the differences in incidence of cesarean and other important perinatal outcomes; and (4) data from multiple ongoing RCTs of ECV under inhalational and intravenous anesthesia are not available, and the data synthesis based on current published studies may be skewed. Finally, neither the parturient nor the clinicians were blinded for type of anesthesia interventions in the trials; this may increase the risk of observer bias.

In conclusion, despite the pain relief from all the anesthesia interventions and the increased procedure success rate associated with neuraxial anesthesia, the involvement of anesthesia management in ECV did not significantly reduce the incidence of cesarean delivery. The decision to proceed with or without anesthesia intervention should be made on an individual basis.

DISCLOSURES

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