Neuraxial analgesia to increase the success rate of external cephalic version: a systematic review and meta-analysis of randomized controlled trials

Elena Rita Magro-Malosso, MD; Gabriele Saccone, MD; Mariarosaria Di Tommaso, MD; Michele Mele, MD; Vincenzo Berghella, MD

BACKGROUND: External cephalic version is a medical procedure in which the fetus is externally manipulated to assume the cephalic presentation. The use of neuraxial analgesia for facilitating the version has been evaluated in several randomized clinical trials, but its potential effects are still controversial.

OBJECTIVE: The objective of the study was to evaluate the effectiveness of neuraxial analgesia as an intervention to increase the success rate of external cephalic version.

DATA SOURCES: Searches were performed in electronic databases with the use of a combination of text words related to external cephalic version and neuraxial analgesia from the inception of each database to January 2016.

STUDY ELIGIBILITY CRITERIA: We included all randomized clinical trials of women, with a gestational age ≥36 weeks and breech or transverse fetal presentation, undergoing external cephalic version who were randomized to neuraxial analgesia, including spinal, epidural, or combined spinal-epidural techniques (ie, intervention group) or to a control group (either intravenous analgesia or no treatment).

STUDY APPRAISAL AND SYNTHESIS METHODS: The primary outcome was the successful external cephalic version. The summary measures were reported as relative risk or as mean differences with a 95% confidence interval.

TABULATION, INTEGRATION, AND RESULTS: Nine randomized clinical trials (934 women) were included in this review. Women who received neuraxial analgesia had a significantly higher incidence of successful external cephalic version (58.4% vs 43.1%; relative risk, 1.44, 95% confidence interval, 1.27–1.64), cephalic presentation in labor (55.1% vs 40.2%; relative risk, 1.37, 95% confidence interval, 1.08–1.73), and vaginal delivery (54.0% vs 44.6%; relative risk, 1.21, 95% confidence interval, 1.04–1.41) compared with those who did not. Women who were randomized to the intervention group also had a significantly lower incidence of cesarean delivery (46.0% vs 55.3%; relative risk, 0.83, 95% confidence interval, 0.71–0.97), maternal discomfort (1.2% vs 9.3%; relative risk, 0.12, 95% confidence interval, 0.02–0.99), and lower pain, assessed by the visual analog scale pain score (mean difference, −4.52 points, 95% confidence interval, −5.35 to 3.69) compared with the control group. The incidences of emergency cesarean delivery (1.6% vs 2.5%; relative risk, 0.63, 95% confidence interval, 0.24–1.70), transient bradycardia (11.8% vs 8.3%; relative risk, 1.42, 95% confidence interval, 0.72–2.80), nonreassuring fetal testing, excluding transient bradycardia, after external cephalic version (6.9% vs 7.4%; relative risk, 0.93, 95% confidence interval, 0.53–1.64), and abruption placentae (0.4% vs 0.4%; relative risk, 1.01, 95% confidence interval, 0.06–16.1) were similar.

CONCLUSION: Administration of neuraxial analgesia significantly increases the success rate of external cephalic version among women with malpresentation at term or late preterm, which then significantly increases the incidence of vaginal delivery.

Key words: anesthesia, breech, cesarean delivery, delivery, version, vertex

The management of a woman with term malpresentation has undergone major changes during the last few years, with planned cesarean delivery being recommended,[1] based on randomized clinical trial data.[2] Such changes have made breech presentation one of the most common causes of the rise in cesarean delivery rates.[1]

External cephalic version is a medical procedure in which the fetus with malpresentation, breech or transverse, is externally manipulated to assume the cephalic presentation. External cephalic version has been associated with a significant reduction in breech presentation at delivery and consequently the rate of cesarean deliveries.[3]

From the Department of Health Science, Division of Pediatrics, Obstetrics, and Gynecology, Careggi Hospital University of Florence, Florence, Italy (Drs Magro-Malosso and Di Tommaso); Department of Neuroscience, Reproductive Sciences, and Dentistry, School of Medicine, University of Naples Federico II, Naples, Italy (Dr Saccone); and Department of Anesthesiology (Dr Mele) and Division of Maternal-Fetal Medicine (Dr Berghella), Department of Obstetrics and Gynecology, Sidney Kimmel Medical College of Thomas Jefferson University, Philadelphia, PA.

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Corresponding author: Vincenzo Berghella, MD. vincenzo.berghella@jefferson.edu

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Several interventions have been evaluated to try to increase the success of external cephalic version. Among these, for example, tocolysis has been associated with a significant increase in cephalic presentation in labor and decrease in cesarean delivery.[4-6] The use of neuraxial analgesia has also been evaluated in several published randomized clinical trials[7-15] to try to increase the success of external cephalic version, but its potential benefits are still controversial.

Materials and Methods

Objective

The aim of this systematic review and meta-analysis of randomized clinical trials was to evaluate the effectiveness of neuraxial analgesia as intervention to increase the success rate of external cephalic version.

Search strategy

This metaanalysis was performed according to a protocol recommended for systematic review.[16] The review protocol was designed a priori defining methods for collecting, extracting and analyzing data. The research was conducted using MEDLINE, EMBASE, Web of Sciences, Scopus, ClinicalTrial.gov, OVID, and Cochrane Library as electronic databases. The trials were identified with the use of a combination of the following text words: external cephalic version, anesthesia, analgesia, spinal, epidural, anesthetic interventions, obstetric anesthesia, regional anesthesia, and randomized from the inception of each database to January 2016. No restrictions for language or geographic location were applied.

Study selection

We included all randomized clinical trials of women with breech and/or transverse presentation undergoing external cephalic version who were randomized to neuraxial analgesia, including spinal analgesia, epidural analgesia, or combined spinal-epidural technique (ie, intervention group) or to intravenous analgesia or no anesthetic treatment (control group). We therefore included both studies comparing neuraxial analgesia vs intravenous analgesia and studies comparing neuraxial analgesia vs no anesthetic intervention. Only women with gestational age at or greater than 36 weeks were included. Quasirandomized trials (ie, trials in which allocation was done on the basis of a pseudorandom sequence, eg odd/even hospital number or date of birth, alternation) were excluded.

Data extraction and risk of bias assessment

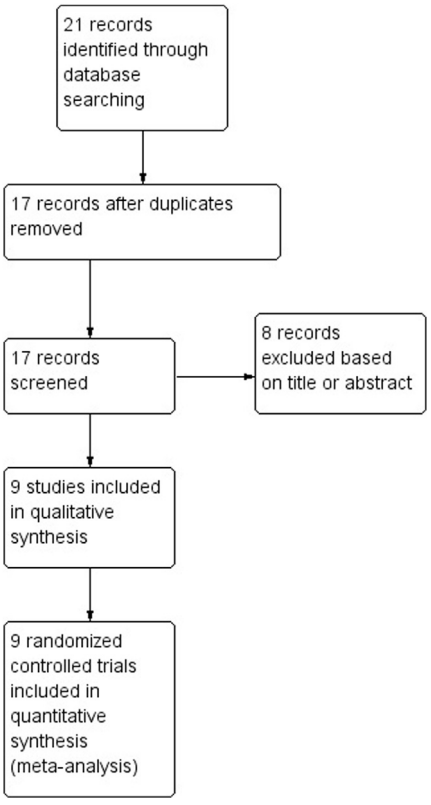
The risk of bias in each included study was assessed by using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions*.[16] Seven domains related to risk of bias were assessed in each included trial because there is evidence that these issues are associated with biased estimates of treatment effect including the following: (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessment; (5) incomplete outcome data; (6) selective reporting; and (7) other bias. Review authors' judgments were categorized as low risk, high risk, or unclear risk of bias.[16]

All analyses were done using an intention-to-treat approach, evaluating women according to the treatment group to which they were randomly allocated in the original trials. The primary outcome was successful external cephalic version, defined as the percentage of fetuses that were externally rotated from breech or transverse presentation to a vertex presentation at external cephalic version.

Secondary outcomes were incidence of cesarean delivery, vaginal delivery, vaginal breech delivery, emergency cesarean delivery, fetal morbidity (transient bradycardia and nonreassuring fetal testing after external cephalic version), maternal discomfort, maternal pain score, and incidence of abruption placentae.

Data from each eligible study were extracted without modification of original data onto custom-made data collection forms. Two authors (E.R.M.-M. and G.S.) independently assessed inclusion criteria, risk of bias, and data extraction. Disagreements were resolved by consensus through a discussion with a third reviewer (V.B.).

FIGURE 1
Flow diagram of studies identified in the systematic review



The Prisma template indicates the Preferred Reporting Item for Systematic Reviews and Meta-Analyses.

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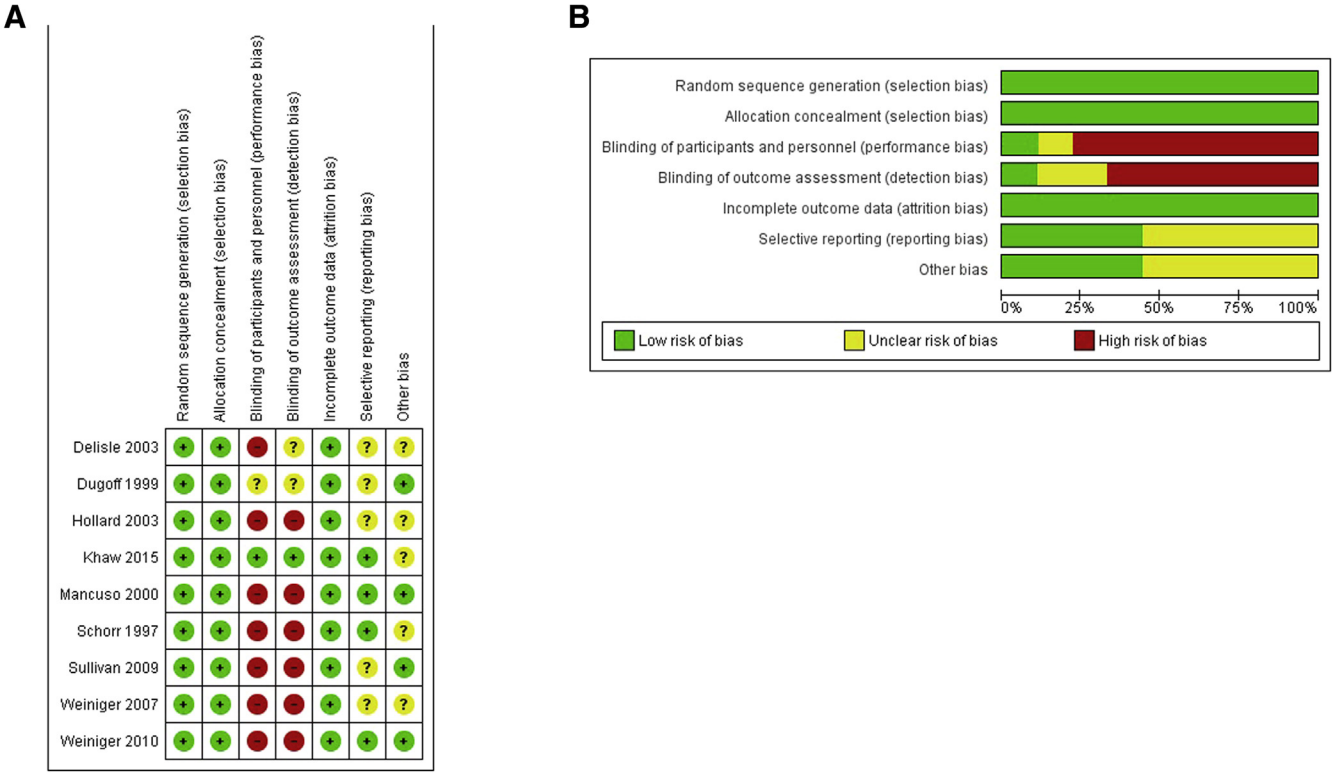
Data not presented in the original publications were requested from the principal investigators.

We planned to assess the primary outcome (ie, successful external cephalic version) in subgroup analyses according to the type of control (either intravenous analgesia or no anesthetic intervention) and also according to the type of neuraxial technique (spinal vs epidural). We also performed a sensitivity analysis according to the risk of bias of the included trials.

Data analysis

The data analysis was completed independently by 2 authors (E.R.M.-M. and G.S.) using Review Manager 5.3 (The Nordic Cochrane Center,

FIGURE 2
Assessment of risk of bias



A, Summary of the risk of bias for each trial. The *plus sign* indicates a low risk of bias; the *minus sign* indicates a high risk of bias; the *question mark* indicates an unclear risk of bias. **B,** Risk of bias graph about each risk of bias item presented as percentages across all included studies.

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Cochrane Collaboration, 2014; Copenhagen, Denmark). The completed analyses were then compared, and any difference was resolved with review of the entire data and independent analysis.

Between-study heterogeneity was explored using the I^2 statistic, which represents the percentage of between-study variation that is due to heterogeneity rather than chance. A value of 0% indicates no observed heterogeneity, whereas I^2 values of $\geq$50% indicate a substantial level of heterogeneity. A fixed-effects model was used if substantial statistical heterogeneity was not present. On the contrary, if there was evidence of significant heterogeneity between studies included, a random-effect model was used.[16] Potential publication biases were assessed statistically by using Begg's and Egger's tests.[16] A value of $P < .05$ was considered statistically significant.

Tests for funnel plot asymmetry were carried out only with an exploratory aim when the total number of publications included for each outcome was less than 10. In this case, the power of the tests is too low to distinguish chance from real asymmetry. The summary measures were reported as relative risk or as mean differences with 95% confidence interval.

The metaanalysis was reported following the Preferred Reporting Item for Systematic Reviews and Meta-Analyses statement.[17] Before data extraction, the review was registered with the International Prospective Register of Systematic Reviews (registration number CRD42016036363).

Results

Study selection and study characteristics

Figure 1 shows the flow diagram (Preferred Reporting Item for Systematic Reviews and Meta-Analyses template) of information derived from the reviewing of potentially relevant articles. Nine randomized clinical trials (934 women), meeting inclusion criteria, were included in this review.[7-15] Two studies were published in abstract form only.[10,11]

Tests for funnel plot asymmetry were carried out only with an exploratory aim because the total number of publications included for each outcome was less than 10. Despite this, the quality of the randomized clinical trials included in our metaanalysis assessed by the Cochrane Collaboration's tool was high.[16] All the included studies had low risk of bias in allocation concealment, random sequence generation, and incomplete outcome data. In 3 of the included randomized clinical trials, all investigators were blinded for anesthetic intervention to the randomization (Figure 2).[7,8,15]

TABLE 1
Characteristics of the included trials

Characteristics	Schorr et al, 1997[7]	Dugoff et al, 1999[8]	Mancuso et al, 2000[9]	Hollard et al, 2003[10]	Delisle et al, 2003[11]	Weiniger et al, 2007[12]	Sullivan et al, 2009[13]	Weiniger et al, 2010[14]	Khaw et al, 2015[15]
Study location	Mississippi	Colorado	Hawaii	California	British Columbia	Israel	Illinois	Israel	China
Sample size	69 (35/34)	102 (50/52)	108 (54/54)	36 (17/19)	201 (99/102)	70 (36/34)	95 (48/47)	64 (31/33)	189 (63/63/63)[a]
Type of malpresentation	Breech 31/35 (88.6%) vs 29/34 (85.3%) transverse 4/35 (11.4%) vs 5/34 (14.7%)	Breech	Breech 50/54 (92.6%) vs 49/54 (90.7%) transverse 4/54 (7.4%) vs 5/54 (9.3%)	Breech	Nonvertex	Breech	Breech	Breech	Breech
GA at ECV, wks	>37	>36	≥37	>36	>36	37–40	≥36	37–40	At term
Regional analgesia (epidural and/or spinal)	Epidural, 2%, lidocaine with 1:200,000 epinephrine	Spinal, 10 μg sufentanil and 1 mL of 0.25% bupivacaine	Epidural, 2% lidocaine with 1:200,000 epinephrine and 100 μg of fentanyl	Spinal, 6 mg of 2% lidocaine and 15 μg fentanyl	Spinal, 2.5 mg bupivacaine and 20 μg fentanyl	Spinal, 7.5 mg bupivacaine	Spinal: 2.5 mg bupivacaine and 15 μg fentanyl Epidural: 45 mg lidocaine and 15 μg epinephrine	Spinal: 7.5 mg bupivacaine	Spinal: 9 mg bupivacaine and 15 μg remifentanil (group 1)
Control group	No anesthetic intervention	No anesthetic intervention	No anesthetic intervention	No anesthetic intervention	No anesthetic intervention	No anesthetic intervention	IVA	No anesthetic intervention	IVA (group 2) No anesthetic intervention (group 3)
IVA	—	—	—	—	—	—	50 μg fentanyl	—	0.1 μg/kg remifentanil
Blinded	All investigators were blinded	All investigators were blinded	Not reported	Operators were not blinded	Not reported	The 2 obstetricians were not blinded	Obstetricians were not blinded	The two obstetricians were not blinded	Operators were blinded
Tocolysis	0.25 mg terbutaline, SC	0.25 mg terbutaline i.v.	0.25 mg terbutaline SC	0.25 mg terbutaline SC	Nitroglycerin i.v.	Ritodrine 50 mg i.v./ nifedipine 20 mg SL[b]	0.25mg Terbutaline i.v.	Ritodrine 50mg i.v. / nifedipine 20 mg SL[b]	10 μg hexoprenaline i.v.
Hydration before anesthesia	2000 mL Ringer's solution	500 mL Ringer's solution	1500 mL Ringer's solution	1000 mL Ringer's solution	At the discretion of the attending anesthesiologist	1000 mL Ringer's solution	500 mL Ringer's solution	1000 mL Ringer's solution	500 mL Hartmann's solution
Number of maximum attempts at ECV	3	4	3	2.1 ± 1.4 vs 2.6 ± 1.4[c]	4	3	Not reported	3	5
Number of operators	Not reported	Not reported	2	1	Not reported	2	Not reported	2	2

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(continued)

TABLE 1
Characteristics of the included trials *(continued)*

Characteristics	Schorr et al, 1997[7]	Dugoff et al, 1999[8]	Mancuso et al, 2000[9]	Hollard et al, 2003[10]	Delisle et al, 2003[11]	Weiniger et al, 2007[12]	Sullivan et al, 2009[13]	Weiniger et al, 2010[14]	Khaw et al, 2015[15]
Experience of the operator	Resident physician (third or fourth year) with a MFM fellow in attendance	Staff physician under direct supervision of attending physicians	Resident physician with assistance from experienced attending obstetricians	One MFM physician	Had at least a successful ECV in primiparous without regional anesthesia in the past or resident under supervision	Senior obstetrician (5 y experience with ECV) assisted by another obstetrician	Obstetricians	Senior obstetrician (5 y experience with ECV) assisted by another obstetrician	A pool of 5 obstetric specialists experienced in performing ECV
Primary outcome	Successful ECV	Successful ECV	Successful ECV	Successful ECV	Successful ECV	Successful ECV	Successful ECV	Successful ECV	Successful ECV
Level of anesthesia	Sensory at T6	Sensory at T6	Sensory at T10	Not reported	Sensory at T6	Sensory at T6	Not reported	Sensory at T6	Sensory at T7
Other comments	Transvaginal elevation of the breech								Group 3 with failed ECV was further randomized to receive RA or IVA

Data are presented as total number (number in the regional analgesia group per number in the control group).

ECV, external cephalic version; *GA*, gestational age; *i.v.*, intravenous; *IVA*, intravenous anesthesia; *MFM*, maternal-fetal medicine; *RA*, regional anesthesia *SC*, subcutaneous.

[a] Group 1/group2/group 3: group 1 received spinal analgesia, group 2 received IVA, and group 3 received no anesthetic intervention; [b] Ritodrine has been replaced with nifedipine because of nonavailability of this drug during the study; [c] mean ± SD.

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Publication bias, assessed using Begg's and Egger's tests, was not significant ($P = .77$ and $P = .64$, respectively). Statistical heterogeneity within the trials was low, with no inconsistency in the risk estimate for the primary outcome. Unpublished data were provided by one author.[10]

Table 1 shows the characteristics of the included trials. Table 2 shows inclusion and exclusion criteria. Characteristics of the women included (maternal age, gestational age at external cephalic version, parity and anterior placenta location) were reported in Table 3. All studies randomized women with singleton breech or transverse presentations at term or late-preterm (≥36 weeks) and no contraindications to external cephalic version.

All randomized clinical trials used a tocolytic drug in both groups and hydration before the anesthetic intervention. Tocolytic therapy differed in the type of agent used and in route of administration: 3 trials used subcutaneous terbutaline,[7,9,10] 2 trials used intravenous terbutaline,[8,13] 1 used intravenous hexoprenaline,[15] 1 used intravenous nitroglycerine,[11] and 2 studies[12,14] used intravenous ritodrine, which was replaced with sublingual nifedipine after 8 months because of nonavailability of this drug during the study.

One study compared neuraxial analgesia with intravenous analgesia[13]; 7 trials compared neuraxial analgesia with no anesthetic intervention.[7-12,14] The trial of Khaw et al[15] was a double-phased, 3-armed randomized blinded study: in phase I, 189 women were randomized to external cephalic version under either spinal anesthesia, intravenous analgesia, or no anesthetic interventions (control group); in phase II, women in the control group in whom the initial external cephalic version failed were further randomized to receive either spinal analgesia (n = 9) or intravenous analgesia (n = 9) for a reattempt. We therefore excluded the phase II from our metaanalysis.

Regarding the intervention, 6 studies addressed the effect of spinal analgesia on external cephalic version[8,10-12,14,15];

TABLE 2
Inclusion and exclusion criteria of the included trials

Study	Inclusion criteria	Exclusion criteria
Schorr et al, 1997[7]	GA >37 wks	Placenta previa, evidence of fetal compromise, IUGR, PROM
Dugoff et al, 1999[8]	GA ≥36 wks, breech presentation (not transverse or oblique lie); reactive NST; intact membranes with a minimum 2 × 2 cm pocket of amniotic fluid	Gross fetal anomalies, uterine malformation, EFW >4000 g, IUGR, placenta previa; known maternal history of third-trimester vaginal bleeding; labor, no contraindications to spinal anesthesia or terbutaline
Mancuso et al, 2000[9]	At least 18 y with singleton pregnancies of at least 37 wks in breech or transverse presentations, intact membranes, EFW between 2000 and 4000 g, reassuring FHR testing	Placenta previa, prior classical CD, third-trimester bleeding, AFI <5 cm or >25 cm, known uterine malformation, uncontrolled hypertension, suspected major fetal anomaly, active-phase labor
Hollard et al, 2003[10]	Singleton gestation, breech presentation, GA >36 wks, not in labor, reactive fetal heart rate	Uteroplacental insufficiency, third-trimester bleeding, IUGR, AFI <6, uterine malformations, placenta previa, maternal cardiac or hypertensive disease, PROM, fetal anomaly, EFW >4500 g, previous uterine surgery, maternal obesity >50% of IBW
Delisle et al, 2003[11]	Singleton fetuses in a nonvertex presentation, maternal age of at least 18, GA ≥36 wks, intact membranes, reactive NST	Not reported in abstract
Weiniger et al, 2007[12]	ASA status I-II, GA 37−40 wks, no fetal abnormality	Previous uterine surgery or uterine anomaly, contraindication for vaginal delivery and for regional analgesia, patient refusal of regional analgesia, neuropathy, severe back pain with neurological radiation, poor communication, BMI ≥40 kg/m^2
Sullivan et al, 2009[13]	GA ≥36 wks, singleton pregnancies, willing to receive either CSE analgesia or systemic opioid analgesia for ECV	Contraindications to neuraxial anesthesia or allergies to any study medication
Weiniger et al, 2010[14]	ASA status I-II, GA 37−40 wks, no fetal abnormality (including IUGR), no contraindication for vaginal delivery and for regional analgesia	Previous CD, previous myomectomy with uterine cavity penetration or uterine anomaly, BMI ≥40 kg/m^2, AFI <7 cm, neuropathy, severe back pain with radicular radiation, request for elective CD
Khaw et al, 2015[15]	ASA status I-II, term parturients, breech-presenting fetus	Contraindications to ECV including patients with known uterine scar or anomaly, unexplained third-trimester bleeding, obstetric or medical conditions complicating pregnancy, compromised fetus, nuchal cord, fetal anomaly, PROM, labor

AFI, amniotic fluid index; *ASA*, American Society of Anesthetists, *BMI*, body mass index; *CD*, cesarean delivery; *CSE*, combined spinal-epidural; *EC*, external cephalic version; *ECV*, external cephalic version; *EFW*, estimated fetal weight; *FHR*, fetal heart rate; *GA*, gestational age; *IBW*, ideal body weight, *IUGR*, intrauterine growth restriction; *NST*, nonstress test; *PROM*, premature rupture of membranes.

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2 studies assessed the effect of epidural.[7,9] Sullivan et al[13] used a combined spinal-epidural technique.

Of the 934 singletons included in the metaanalysis, 433 (46.4%) were randomized to the neuraxial analgesia group (ie, intervention group) and 501 (53.6%) to the control group (either intravenous analgesia or no anesthetic intervention).

Synthesis of results

Table 4 shows the pooled data of the primary and the secondary outcomes of the metaanalysis. Women who received neuraxial techniques had a significantly higher incidence of successful external cephalic version (58.4% vs 43.1%; relative risk, 1.44, 95% confidence interval, 1.27−1.64) (Figure 3), cephalic presentation in labor (55.1% vs 40.2%; relative risk, 1.37, 95% confidence interval, 1.08−1.73), and vaginal delivery (54.0% vs 44.6%; relative risk, 1.21, 95% confidence interval, 1.04−1.41) compared with those who did not.

Women who were randomized to the intervention group had also a significantly lower incidence of cesarean delivery (46.0% vs 55.3%; relative risk, 0.83, 95% confidence interval, 0.71−0.97), maternal discomfort (1.2% vs 9.3%; relative risk, 0.12, 95% confidence interval, 0.02−0.99), and lower pain, assessed by the visual analog scale pain score (mean differences, −4.52 point 95% confidence interval, −5.35 to 3.69) compared with the control group.

The incidences of emergency cesarean delivery (1.6% vs 2.5%; relative risk, 0.63, 95% confidence interval, 0.24−1.70), transient bradycardia (11.8% vs 8.3%; relative risk, 1.42, 95% confidence interval, 0.72−2.80), nonreassuring fetal testing, excluding transient bradycardia, after external cephalic version (6.9% vs 7.4%; relative risk, 0.93, 95% confidence interval, 0.53−1.64), and abruptio placentae (0.4% vs 0.4%; relative risk, 1.01, 95% confidence

TABLE 3
Characteristics of the women included in the trials

Characteristics	Schorr et al, 1997[7]	Dugoff et al, 1999[8]	Mancuso et al, 2000[9]	Hollard et al, 2003[10]	Delisle et al, 2003[11]	Weiniger et al, 2007[12]	Sullivan et al, 2009[13]	Weiniger et al, 2010[14]	Khaw et al, 2015[15]
Maternal age, y, mean ± SD or median [range]	27.7 ± 6.1 vs 25.8 ± 6.6	24.3 ± 0.9 vs 26.8 ± 0.9	28.5 ± 4.8 vs 28.2 ± 4.8	29.8 ± 4.9 vs 29.3 ± 4.9	Not reported[a]	24.6 ± 3.8 vs 28.1 ± 4.1	32 [27–35] vs 33 [30–36]	28.5 [21–40] vs 28.6 [20–36]	32 [23–42] vs 32 [20–42]
GA at ECV, wks, mean ± SD or median [range]	38.0 ± 2.3 vs 37.4 ± 2.1	38.0 ± 0.2 vs 38.0 ± 0.2	38.1 ± 1.2 vs 37.9 ± 1.0	38.0 ± 8 vs 37.4 ± 5	37.4 (37.2–37.4) vs 37.2 (37.0–37.5)[b]	37.9 ± 1.0 vs 37.9 ± 1.0	37 [37–38] vs 37 [37–38]	38.1 ± 0.9 vs 38.2 ± 1.1	36.9 [36.6–39.2] vs 36.6 [36.1–39.6]
Multiparous n, %, or mean ± SD or median [range]	21/35 (60%) vs 18/34 (53%)	1.5 ± 0.0 vs 1.6 ± 0.1	24/54 (44%) vs 25/54 (46%)	9/17 (53%) vs 13/19 (68%)	39/99 (39.4%) vs 39/102 (38.2%)	0/36 vs 0/34	18/48 (62%) vs 18/47 (38%)	31/31 (100%) vs 33/33 (100%)	1 [0–3] vs 1 [0–4]
Anterior placenta, n, %	13/35 (37%) vs 11/34 (32%)	23/50 (46%) vs 22/52 (42%)	20/54 (37%) vs 18/54 (33%)	6/17 (35%) vs 10/19 (53%)	Not reported	14/36 (39%) vs 14/34 (41%)	Not reported	11/31 (35%) vs 17/33 (51%)	Not reported

Data are presented as number in the regional analgesia group vs number in the control group.

ECV, external cephalic version; *GA*, gestational age.

[a] Delisle et al reported a similar maternal age in both groups; [b] The 95% confidence intervals are in parentheses.

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interval, 0.06–16.1) were not significantly different.

Subgroup analysis of the primary outcome (ie, successful external cephalic version) concurred with the overall analysis for the following:

1. Studies in which control was intravenous analgesia[13]: relative risk, 1.54, 95% confidence interval, 1.22–2.63.
2. Studies in which the control was no anesthetic intervention[7-12,14]: relative risk, 1.50, 95% confidence interval, 1.26–1.77.
3. Studies in which spinal anesthesia was used as neuraxial analgesia[8,10-12,14,15]: relative risk, 1.34, 95% confidence interval, 1.17–1.54.
4. Studies in which epidural analgesia was used as neuraxial analgesia[7,9]: relative risk, 1.91, 95% confidence interval, 1.36–2.68.
5. The successful external cephalic version rate was still significantly higher in the neuraxial analgesia group and also in the sensitivity analysis of trials with no high risk of bias items (Figure 2) according to the Cochrane Risk of bias tools (relative risk, 1.23, 95% confidence interval, 1.03–1.46).[8,15]

Moreover, by using an indirect comparison metaanalysis, we found no differences in the successful rate of external cephalic version comparing spinal analgesia with epidural analgesia (relative risk, 1.17, 95% confidence interval, 0.72–1.91).

Comment

Main findings

This metaanalysis from 9 carefully conducted and low risk of bias randomized clinical trials, including 934 singleton pregnancies with malpresentation (either breech or transverse presentation) at term or late preterm (≥36 weeks), showed that the administration of neuraxial analgesia in addition to a tocolytic drug significantly increased the success rate of external cephalic version compared with a tocolytic drug alone.

Pooled results showed a positive effect of neuraxial analgesia on reducing the cesarean delivery, maternal discomfort,

TABLE 4
Primary and secondary outcomes

Outcomes	Schorr et al, 1997[7]	Dugoff et al, 1999[8]	Mancuso et al, 2000[9]	Hollard et al, 2003[10]	Delisle et al, 2003[11]	Weiniger et al, 2007[12]	Sullivan et al, 2009[13]	Weiniger et al, 2010[14]	Khaw et al, 2015[15]	Total	I^2	RR or MD (95% CI)
Successful ECV	24/35 (68.6%) vs 11/34 (32.3%)	22/50 (44.0%) vs 22/52 (42.3%)	32/54 (59.2%) vs 18/54 (33.3%)	9/17 (52.9%) vs 10/19 (52.6%)	41/99 (41.4%) vs 31/102 (33.7%)	24/36 (66.6%) vs 11/34 (32.3%)	22/48 (45.8%) vs 14/47 (30.0%)	27/31 (87.0%) vs 19/33 (57.6%)	52/63 (82.5%) vs 80/126 (63.5%)	253/433 (58.4%) vs 216/501 (43.1%)	16%	**1.44 (1.27–1.64)**
Cephalic presentation in labor	24/35 (68.6%) vs 10/34 (29.4%)	20/50 (40%) vs 26/52 (50%)	32/54 (59.2%) vs 19/54 (35.2%)	10/17 (58.8%) vs 9/19 (47.4%)	Not reported	Not reported	Not reported	Not reported	Not reported	86/156 (55.1%) vs 64/159 (40.2%)	75%	**1.37 (1.08–1.73)**
Vaginal delivery	23/35 (65.7%) vs 7/34 (20.6%)	16/50 (32.0%) vs 25/52 (48.1%)	29/54 (53.7%) vs 17/54 (31.5%)	9/17 (52.9%) vs 8/19 (42.1%)	Not reported	Not reported	17/48 (36.0%) vs 12/47 (25.0%)	27/31 (87.1%) vs 30/33 (91.0%)	40/63 (63.5%) vs 64/126 (51.0%)	161/298 (54.0%) vs 163/365 (44.6%)	91%	**1.21 (1.04–1.41)**
Vaginal breech delivery	Not reported	0/50 (0.0%) vs 0/52 (0.0%)	1/54 (1.8%) vs 3/54 (5.5%)	0/17 (0.0%) vs 0/19 (0.0%)	Not reported	Not reported	0/48 (0.0%) vs 0/47 (0.0%)	0/31 (0.0%) vs 3/33 (9.1%)	Not reported	1/102 (0.98%) vs 6/106 (5.6%)	0%	1.17 (0.02–1.41)
CD	12/35 (34.3%) vs 27/34 (79.4%)	34/50 (68.0%) vs 27/52 (51.9%)	25/54 (46.3%) vs 37/54 (68.5%)	8/17 (47.0%) vs 11/19 (57.9%)	Not reported	Not reported	31/48 (64.0%) vs 35/47 (75.0%)	4/31 (12.9%) vs 3/33 (9.1%)	23/63 (36.5%) vs 62/126 (49.2%)	137/298 (46.0%) vs 202/365 (55.3%)	75%	**0.83 (0.71–0.97)**
Emergency CD within 24 hours of ECV	Not reported	0/50 (0.0%) vs 1/52 (1.9%)	0/54 (0.0%) vs 0/54 (0.0%)	1/17 (5.9%) vs 0/19 (0.0%)	1/73 (1.4%) vs 0/68 (0.0%)	0/36 (0.0%) vs 0/34 (0.0%)	1/48 (2.1%) vs 1/47 (2.1%)	0/31 (0.0%) vs 0/33 (0.0%)	3/63 (4.8%) vs 9/126 (7.14%)	6/372 (1.6%) vs 11/433 (2.5%)	0%	0.63 (0.24–1.70)
Transient bradycardia	Not reported	11/50 (22.0%) vs 6/52 (12.0%)	2/54 (3.7%) vs 3/54 (5.5%)	3/17 (17.6%) vs 3/19 (15.8%)	Not reported	Not reported	Not reported	2/31 (6.4%) vs 1/33 (3.0%)	Not reported	18/152 (11.8%) vs 13/156 (8.3%)	45%	1.42 (0.72–2.80)
Nonreassuring fetal testing (excluding transient bradycardia) after ECV	Not reported	0/50 (0.0%) vs 1/52 (1.9%)	Not reported	1/17 (5.9%) vs 0/19 (0.0%)	1/73 (1.4%) vs 0/68 (0.0%)	2/36 (5.5%) vs 0/34 (0.0%)	14/48 (29.2%) vs 13/47 (27.6%)	1/31 (3.0%) vs 0/33 (0.0%)	3/63 (4.8%) vs 9/126 (7.1%)	22/318 (6.9%) vs 23/311 (7.4%)	15%	0.93 (0.53–1.64)
Maternal discomfort	1/35 (2.8%) vs 4/34 (11.8%)	0/50 (0.0%) vs 4/52 (8.0%)	Not reported	Lower in RA group	Not reported	Lower in RA group	Lower in RA group	Lower in RA group	Lower in RA group	1/85 (1.2%) vs 8/86 (9.3%)	0%	**0.12 (0.02–0.99)**

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(continued)

TABLE 4
Primary and secondary outcomes *(continued)*

Outcomes	Schorr et al, 1997[7]	Dugoff et al, 1999[8]	Mancuso et al, 2000[9]	Hollard et al, 2003[10]	Delisle et al, 2003[11]	Weiniger et al, 2007[12]	Sullivan et al, 2009[13]	Weiniger et al, 2010[14]	Khaw et al, 2015[15]	Total	I^2	RR or MD (95% CI)
Maternal pain score	Not reported	Not reported	Not reported	2.3 ± 2.6 vs 7.2 ± 2.8[a]	Not reported	1.76 ± 2.7 vs 6.84 ± 3.1[a]	3 [0–12] vs 36 [16–54][b]	1.7 ± 2.4 vs 5.5 ± 2.9[a]	0 [0–0] vs 35 [0–60] vs 50 [30–75][b]	—	0%	**−4.52 point (−5.35 to 3.69)**
Abruption placentae	0/35 (0.0%) vs 0/34 (0.0%)	0/50 (0.0%) vs 1/52 (1.9%)	0/54 (0.0%) vs 0/54 (0.0%)	1/17 (5.9%) vs 0/19 (0.0%)	Not reported	0/36 (0.0%) vs 0/34 (0.0%)	Not reported	0/31 (0.0%) vs 0/33 (0.0%)	Not reported	1/223 (0.4%) vs 1/226 (0.4%)	0%	1.01 (0.06–16.1)

Data are presented as the number in the regional analgesia group vs the number in the control group. Boldfaced data indicate they are statistically significant.

ECV, external cephalic version; *CD*, cesarean delivery; *NST*, non-stress test; *RR*, relative risk; *MD*, mean difference; *CI*, confidence interval.

[a] Pain score on a visual analog scale (0–10), mean ± SD; [b] Median [interquartile range] pain score on a visual analog scale (range 0–100).

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and maternal pain and also a positive effect on increasing the rate of cephalic presentation in labor and thus the rate of vaginal delivery. Our metaanalysis represents level 1 data and included well-designed and high-quality studies. A test of heterogeneity and subgroup analyses all point to the efficacy of neuraxial analgesia as studies so far.

Comparison with existing literature

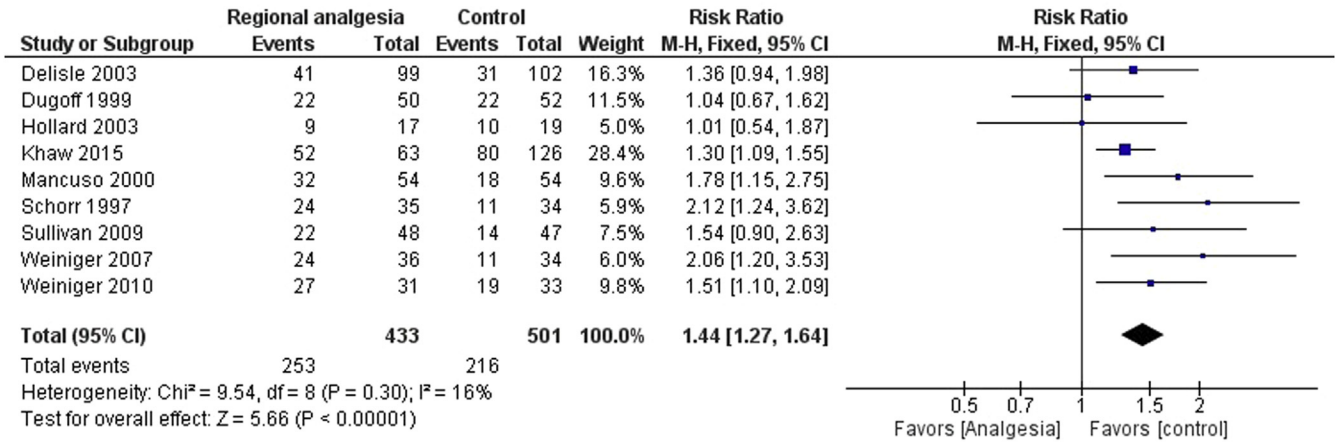
In 2015, a Cochrane review analyzed possible interventions for helping to turn term breech babies to cephalic presentation with external cephalic version.[4] The authors found an increase of the rate of successful external cephalic version with regional analgesia in combination with tocolytic therapy compared with tocolysis alone, but no difference was identified in cesarean delivery. However this metaanalysis did not include all currently available randomized clinical trials.

Strengths and limitations

One of the strengths of our study is the inclusion of only randomized clinical trial data on external cephalic version in a specific population (ie, singleton gestations at term or near term with malpresentation). Our metaanalysis included all studies published so far on the topic and studies of high quality and with a low risk of bias according to the Cochrane risk of bias tools. To our knowledge, no prior metaanalysis on this issue is as large, up to date, or comprehensive. The protocol of this review was a priori registered on the International Prospective Register of Systematic Reviews. Statistical tests showed no significant potential publication biases. An intent-to-treat analysis was used, and both random and mixed-effects models were used when appropriate. These are key elements that are needed to evaluate the reliability of a metaanalysis.[16] All included women received tocolytics at external cephalic version, which should be done, given their benefit.[4]

Limitations of our study are inherent to the limitations of the included randomized clinical trials. The randomized clinical trials included in this

FIGURE 3
Forest plot for successful of external cephalic version



CI, confidence interval; *M-H*, Mantel-Haenszel.

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metaanalysis were a mix of neuraxial techniques including epidural, spinal (used most often), and combined spinal-epidural. These individual techniques used different local anesthetics types in varying concentrations and doses. Opioid types and concentrations differed as well. In addition, the level of block obtained was not uniform. All of these variables may have an impact on the outcome and the success of external cephalic version because they can influence perception of maternal pain, abdominal and pelvic muscle relaxation, and anterior abdominal wall muscle relaxation (possibly altering maternal guarding that can occur with external cephalic version and have a negative impact on its success).

The presence of cotreatments and different control groups represent other limitations of this systematic review. Different types and doses of neuraxial analgesia were used, making it unclear which of these should be preferred. Ideally, spinals and epidurals should be compared with each other using uniform drug, opioid type, concentrations, and analgesic level. Most of the included studies were not double blind. This was therefore a considerable source of bias that may have affected treatment of these women or their neonates. In fact, the incidence of successful external cephalic version was slightly lower than usually reported in the control group (43.1%).[1]

Conclusions and implications

Neuraxial analgesia in addition of tocolytic therapy can be considered a reasonable intervention to significantly increase external cephalic version success rate and cephalic presentation in labor and thus the incidence of vaginal delivery, with significantly reduced incidence of cesarean delivery. Neuraxial analgesia before external cephalic version was safe because it was not associated with increased fetal adverse events, including transient bradycardia or other nonreassuring fetal testing, or abruptio placentae. Women who received neuraxial analgesia had less pain and discomfort that those who did not.

Remaining questions are what type of neuraxial anesthesia and what type and dose of anesthetic drug should be used for external cephalic version.

In summary, the administration of neuraxial analgesia significantly increases the success rate of external cephalic version among women with malpresentation at term or late preterm, which then significantly increases the incidence of vaginal delivery. ■

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