OBSTETRICS

Significant reduction in umbilical artery metabolic acidosis after implementation of intrapartum ST waveform analysis of the fetal electrocardiogram

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BACKGROUND: Although the evidence regarding the benefit of using ST waveform analysis of the fetal electrocardiogram is conflicting, ST waveform analysis is considered as adjunct to identify fetuses at risk for asphyxia in our center. Most randomized controlled trials and meta-analyses have not shown a significant decrease in umbilical metabolic acidosis, while some observational studies have shown a gradual decrease of this outcome over a longer period of time. Observational studies can give more insight into the effect of implementation of the ST technology in daily clinical practice.

OBJECTIVE: To evaluate the change in frequency of perinatal intervention and adverse neonatal outcome after the implementation of ST waveform analysis of the fetal electrocardiogram from 2000 to 2013.

STUDY DESIGN: This retrospective longitudinal study was conducted in a tertiary referral center. A total of 19,664 medium- and high-risk singleton pregnancies with fetuses in cephalic presentation, a gestational age of ≥36 weeks, and the intention to deliver vaginally were included. ST waveform analysis of the fetal electrocardiogram was implemented in the year 2000 and by 2010 all deliveries were monitored using this technology. Data were collected on the following perinatal outcomes: fetal blood sampling, mode of delivery, umbilical cord blood gases, Apgar scores, neonatal encephalopathy, and perinatal death. Longitudinal trend analysis was used to detect changes over time in all deliveries monitored by cardiotocography either alone or in adjunct to ST waveform analysis of the fetal electrocardiogram. Logistic regression was used to correct for possible confounders.

RESULTS: The umbilical artery metabolic acidosis rate declined from 2.5% (average rate of 2000 + 2001 + 2002) to 0.4% (average of 2011 + 2012 + 2013) ($P < .001$), which represents an 84% decrease. This decrease largely occurred between 2006 and 2008, during the Dutch randomized trial on fetal electrocardiogram ST waveform analysis. At this time, approximately 20% of deliveries were monitored using this method. Furthermore, there were significant reductions in fetal blood sampling rate ($P < .001$). Overall cesarean and vaginal instrumental deliveries decreased significantly ($P < .001$), but not for fetal distress. There were no changes in the Apgar scores. The incidence of neonatal encephalopathy was significantly lower in the second part of the study (odds ratio 0.39, 95% confidence interval 0.17–0.89).

CONCLUSION: There was an 84% decrease in the incidence of umbilical artery metabolic acidosis in all deliveries between 2000 and 2013. The neonatal encephalopathy rate, fetal blood sampling rate, and the total number of cesarean and vaginal instrumental deliveries also decreased.

Key words: CTG, fetal blood sampling, fetal electrocardiogram, fetal heart rate monitoring, intrapartum fetal surveillance, learning curve, observational studies, umbilical artery metabolic acidosis, real-world observation, ST waveform analysis

Intrapartum fetal monitoring aims to identify fetuses at risk of perinatal asphyxia. Continuous electronic fetal heart rate monitoring using cardiotocography (CTG) was introduced in the 1960s to detect fetal hypoxia. Several studies have shown that CTG was associated with a decrease in umbilical artery metabolic acidosis and hypoxia-related perinatal mortality compared to intermittent auscultation.[1–5] However, other studies did not show neonatal benefit other than a reduction of neonatal seizures.[6,7]

Furthermore, the interpretation of CTG is susceptible to intra- and inter-observer variation.[8–10] Owing to limitations of CTG, there has been a demand for a complementary test to CTG in order to identify those fetuses that are truly at risk of injury and to reduce the rate of unnecessary cesarean deliveries.

The combination of CTG and automated ST waveform analysis of the fetal electrocardiogram (ECG) may be superior as a measure of fetal hypoxic distress. Changes in the ST waveform, either a biphasic ST segment or an increase in the T/QRS ratio, are signs of myocardial ischemia and are associated with fetal hypoxia.[11,12] Changes in the ST waveform generate ST events. The ST clinical guidelines provide a protocol for intervention based on CTG classification and the type and magnitude of the ST event.[13] The aim of ST technology is to improve diagnostic accuracy and in turn reduce unnecessary operative deliveries.

Six randomized trials and 10 meta-analyses comparing CTG in adjunct to fetal ECG ST waveform analysis with CTG alone have been conducted, with conflicting results.[10,14–30] Only the Swedish trial showed a significant reduction in the umbilical artery metabolic acidosis rate.[15,16] Of the 4 meta-analyses including all 6 trials, 2 showed a significant reduction in umbilical artery metabolic acidosis.[10,30]

Cite this article as: Landman AJEMC, Immink-Duijker ST, Mulder EJH, et al. Significant reduction in umbilical artery metabolic acidosis after implementation of intrapartum ST waveform analysis of the fetal electrocardiogram. Am J Obstet Gynecol 2019;221:63.e1-13.

0002-9378/$36.00

https://doi.org/10.1016/j.ajog.2019.02.049

AJOG at a Glance

Why was this study conducted?

To evaluate perinatal intervention rates and adverse neonatal outcome in the 14 years following the introduction of ST waveform analysis of the fetal electrocardiogram for intrapartum monitoring.

Key findings

With time there was an 84% reduction in the incidence of umbilical artery metabolic acidosis. There was also a decrease in the rate of neonatal encephalopathy, fetal blood sampling rate, and overall cesarean and vaginal instrumental deliveries.

What does this add to what is known?

The findings suggest that the introduction of intrapartum ST waveform analysis methodology has resulted in a striking improvement of perinatal outcome. This does not necessarily imply that ST monitoring itself is the reason for the considerably better outcome. Other factors such as training and improved care during the ST randomized trial (Hawthorne effect) may have been more important.

Several observational studies have demonstrated improved perinatal outcome after implementation of ST waveform analysis of the fetal ECG.[31−41] The rate of umbilical artery metabolic acidosis decreased gradually over time with increasing use of ST technology.[32,33,38,41] Studies have also demonstrated that there is a learning period when working with new technology such as ST waveform analysis, during which staff gain experience with its use and increasingly incorporate the guidelines in their clinical decision making.[33,38,41]

Since there is a discrepancy between randomized trial results, which are obtained in a controlled research setting in a specific population, and experience from daily clinical practice,[42] we evaluated the change in the frequency of perinatal interventions and adverse neonatal outcome in the 14 years after implementation of ST waveform analysis for the fetal ECG in intrapartum monitoring in our tertiary referral center.

Materials and Methods

Study population

This retrospective longitudinal study was performed at University Medical Center Utrecht in the Netherlands, a tertiary referral center with approximately 2500 deliveries a year. We evaluated rates of umbilical artery metabolic acidosis, cesarean and instrumental vaginal deliveries, fetal blood sampling, and neonatal outcomes between 2000 and 2013.

All deliveries of medium- and high-risk singleton pregnancies with a fetus in cephalic presentation, a gestational age of ≥36 weeks, and the intention of vaginal delivery were included. Medium- and high-risk pregnancies were defined by the presence of at least 1 of the following factors: preexisting maternal disease, hypertensive disorders, complicated obstetric history, intrauterine growth restriction, ruptured membranes >24 hours, postterm delivery, meconium-stained amniotic fluid, a nonreassuring fetal heart rate at intermittent auscultation by a midwife, induction of labor, failure to progress, or need for analgesia. Fetuses with congenital anomalies were also included. Deliveries were managed by residents or midwives under the supervision of obstetricians. Institutional review board approval was obtained from the University Medical Center in Utrecht.

Fetal surveillance

ST waveform analysis (STAN S21, S31; Neoventa, Mölndal, Sweden) was introduced in our labor ward in July 2000 as part of a European Community multicenter project (European Union Innovation grant, no. IPS-1999-00029).[43] Our hospital was the coordinating center of the Dutch randomized trial on ST waveform analysis, which was conducted from January 2006 until July 2008.[19,20] ST waveform analysis has been used increasingly since the implementation of the first monitor in July 2000. The numbers and types of monitors are listed in Table 1.[43] By April 2010, all 9 delivery rooms were equipped with a fetal ECG ST waveform analysis unit. From that time onward, nearly all deliveries were monitored using this technology. During the trial the use of ST technology was 23.3% (n = 306) in 2006 and 21.0% (n = 251) in 2007. As the use of ST technology was not recorded during the other years, it was expressed as the number of monitors in use.

There were no major (technical) interventions aiming to improve perinatal outcome during the study period. In our hospital it is common practice that all term deliveries receive internal fetal heart rate monitoring after rupture of the membranes (unless there is a contraindication for a scalp electrode). Simultaneous maternal heart rate monitoring was always available, but indications for its use might have been expanded.

Women received continuous electronic fetal monitoring by CTG alone or in adjunct with ST waveform analysis. Labor ward staff were trained and certified to use the ST waveform analysis clinical guidelines,[13] which included CTG interpretation according to the FIGO guidelines.[44] After implementation of the technology in 2000, the training consisted of lectures, the ST waveform analysis textbook, and multimedia-based teaching using previously recorded cases.[42,45] Staff were certified after passing an examination. During the first phase after implementation, an ST waveform analysis expert was always available for assistance during the daytime. Before initiation of the randomized trial, all gynecologists, residents, and midwives received additional training from 4 instructors.[19,20] Thereafter, routine

TABLE 1
History of fetal electrocardiogram ST waveform analysis usage at Wilhelmina Children's Hospital

Time period	Jul '00 – Jun '02	Jul '02 – May '07	Jun '07 – Sep '09	Oct '09 – Nov '09	Dec '09 – Mar '10	Apr '10 – Dec '13
Number and type of units	1 STAN S21	2 STAN S21	2 STAN S21 1 STAN S31	2 STAN S21 2 STAN S31	4 STAN S31	9 STAN S31

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training sessions and daily discussions of difficult cases during the morning report were pursued to maintain compliance with these guidelines.

Fetal blood sampling was available as an additional assessment of the fetal condition for both ST-monitored and CTG-only-monitored labors. The procedure was performed as described by the NICE guideline.[46] From 2000 until 2006 there was no strict protocol for fetal blood sampling and it was performed at the discretion of the obstetrician. Since the beginning of the Dutch randomized trial in 2006, the following indications for fetal blood sampling have been applied in cases where labor was monitored by ST waveform analysis: (1) start of ST-segment recording with an intermediary or abnormal CTG trace; (2) more than 60 minutes of abnormal CTG tracing during the first stage of labor without ST events; and (3) poor ECG signal quality in the presence of an intermediary or abnormal CTG trace. Immediate delivery, or other measures for intrauterine resuscitation, were required when fetal blood sampling was nonreassuring (pH < 7.20). In the event of a borderline result (pH 7.20–7.25), fetal blood sampling was repeated after 30 minutes.

Outcome measures

Umbilical artery and vein samples were routinely obtained after birth. The base deficit in the extracellular fluid was calculated using the Siggaard-Andersen acid base chart algorithm.[47] Arterial and venous samples with a pH difference of <0.03 units were treated as a single vessel sample of venous origin. Severe umbilical artery acidosis (arterial pH < 7.00)[48] and umbilical artery metabolic acidosis (arterial pH < 7.05 and a base deficit in the extracellular fluid > 12 mmol/L) were used as intermediate markers for adverse neonatal outcome. The same definition for metabolic acidosis was used for single-vessel samples.

The number of fetal blood samples was also recorded. Delivery outcomes consisted of cesarean deliveries for fetal distress, vaginal instrumental deliveries for fetal distress, and total cesarean and vaginal instrumental delivery rates.

Apgar scores (1-minute score < 4 and 5-minute score < 7) and neonatal encephalopathy according to the Sarnat and Sarnat grading system were reported as neonatal outcomes (Appendix, Supplemental Table 1.).[49]

Data collection

Data of deliveries from January 1, 2000 to December 31, 2013 were extracted from our digital obstetric patient registration system on the following variables: maternal age at time of delivery, parity, gestational age, postterms (births > 42+0 weeks of gestation), medical indications to deliver under the supervision of an obstetrician, meconium-stained amniotic fluid, induction of labor, use of epidural analgesia, oxytocin augmentation of labor, neonatal sex, and birthweight. Medical indications included maternal disease, hypertensive disorders (chronic hypertension, pregnancy-induced hypertension, [pre] eclampsia), (gestational) diabetes, prelabor rupture of membranes (>24 hours before labor), and intrauterine growth restriction (<10th percentile). Log books and medical records were used to complete the data. Finally, the neonatal charts of all admissions to the Neonatal Intensive Care Unit (level III) were reviewed for cases of intrapartum asphyxia and subsequently scored for the presence of neonatal encephalopathy by a neonatologist (F.G.).

Statistical analysis

All data were analyzed using SPSS version 21 (IBM Corp, Armonk, NY). Trends in the data were identified using the χ^2 test for trend for dichotomous variables, the ANOVA linear trend analysis for continuous values, and the Jonckheere-Terpstra test for continuous nonparametric data. Ranges of outcome measures were derived by calculating the average of both the first (2000–2002) and last 3 years (2011–2013) of the study.

Generalized estimating equations with logistic regression were used to simultaneously account for changes in population characteristics during the study period with a possible confounding effect on the outcome measures (ie, the increasing use of epidural analgesia and oxytocin augmentation of labor), and to adjust for those mothers who had more than 1 delivery during the study. Odds ratios (OR) and 95% confidence intervals (CI) were calculated in reference to the year 2000.

For all analyses probability values of $\alpha < 0.05$ were considered significant.

Results

During the study there were 28,627 deliveries, of which 19,664 met the inclusion criteria. Baseline characteristics are summarized in Table 2.

Over the years, significantly fewer postterm births occurred and there was a significant increase in oxytocin augmentation of labor, induction of labor, and the use of epidural analgesia. The number of mothers with gestational diabetes increased significantly, while there was a significant decrease in maternal hypertensive disorders.

TABLE 2
Baseline characteristics of all singleton pregnancies in cephalic presentation ≥36 weeks of gestational age with intention to deliver vaginally

Characteristics	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	*P* value
Total number of deliveries, n	1953	1808	1804	1914	2040	1948	1947	1774	1944	2196	2340	2326	2381	2252	
Included deliveries, n	1295	1221	1183	1278	1426	1341	1315	1197	1318	1497	1698	1691	1651	1553	
Maternal age at delivery (years)	32 (28–35)	32 (29–35)	32 (28–36)	32 (28–35)	31 (28–35)	32 (28–35)	32 (28–35)	32 (28–35)	32 (28–35)	32 (28–35)	32 (28–35)	32 (28–35)	32 (28–35)	32 (28–35)	.998[b]
Gestational age (days)	282 (274–287)	282 (274–288)	281 (274–287)	282 (275–288)	282 (276–288)	282 (275–289)	282 (275–287)	281 (274–287)	280 (273–287)	281 (274–287)	281 (273–286)	281 (273–287)	281 (274–287)	281 (274–287)	<.001[b]
Postterm (>42+0 weeks)	88 (6.8)	86 (7.0)	89 (7.5)	85 (6.7)	103 (7.2)	100 (7.5)	77 (5.9)	57 (4.8)	41 (3.1)	43 (2.9)	14 (0.8)	24 (1.4)	30 (1.8)	28 (1.8)	<.001[a]
Nulliparous women	621 (48.0)	595 (48.7)	67 (47.9)	619 (48.4)	684 (48.0)	689 (51.4)	705 (53.6)	636 (53.1)	663 (50.3)	761 (50.8)	815 (48.0)	818 (48.4)	800 (48.5)	731 (47.1)	.731[a]
Pregnancy complications															
Hypertensive disorders	187 (14.4)	163 (13.3)	172 (14.5)	204 (16.0)	210 (14.7)	200 (14.9)	200 (15.2)	175 (14.6)	210 (15.9)	217 (14.5)	255 (15.0)	233 (13.8)	125 (7.6)	106 (6.9)	<.001[a]
Diabetes mellitus and gestational diabetes	26 (2.0)	34 (2.8)	50 (4.2)	55 (4.3)	50 (3.5)	57 (4.3)	64 (4.9)	61 (5.1)	68 (5.2)	118 (7.9)	131 (7.7)	197 (11.6)	119 (7.2)	156 (10.0)	<.001[a]
Prelabor rupture of membranes	100 (7.7)	94 (7.7)	115 (9.7)	111 (8.7)	120 (8.4)	126 (9.4)	92 (7.0)	81 (6.8)	84 (6.4)	81 (5.4)	91 (5.4)	75 (4.4)	94 (5.7)	79 (5.1)	<.001[a]
Intrauterine growth restriction	35 (2.7)	20 (1.6)	27 (2.3)	40 (3.1)	36 (2.5)	45 (3.4)	34 (2.6)	38 (3.2)	32 (2.4)	26 (1.7)	39 (2.3)	42 (2.5)	38 (2.3)	36 (2.3)	.438[a]
Meconium-stained amniotic fluid	294 (22.7)	316 (25.9)	326 (27.5)	306 (23.9)	405 (28.4)	367 (27.4)	331 (25.1)	300 (25.1)	320 (24.3)	332 (22.2)	341 (20.1)	340 (20.1)	377 (22.8)	314 (20.2)	<.001[a]
Epidural analgesia	253 (19.5)	203 (16.6)	185 (15.6)	239 (18.7)	271 (19.0)	323 (24.1)	476 (36.2)	315 (26.3)	423 (32.1)	534 (35.6)	694 (40.8)	679 (40.2)	636 (38.5)	611 (39.3)	<.001[a]
Induction of labor	292 (22.5)	237 (19.4)	255 (21.5)	223 (17.4)	232 (16.3)	250 (18.6)	270 (20.5)	250 (20.9)	334 (25.3)	473 (31.6)	626 (36.9)	592 (35.0)	467 (28.3)	449 (28.9)	<.001[a]
Oxytocin augmentation	70 (5.4)	72 (5.9)	92 (7.8)	151 (11.8)	187 (13.1)	126 (9.4)	161 (12.2)	173 (14.5)	235 (18.2)	435 (29.0)	473 (27.8)	492 (29.1)	547 (33.1)	536 (34.5)	<.001[a]
Neonatal female sex	663 (51.2)	563 (46.1)	558 (47.2)	611 (47.8)	698 (51.1)	645 (48.1)	614 (46.7)	591 (49.4)	605 (45.9)	772 (51.5)	856 (49.6)	811 (48.0)	741 (44.9)	724 (46.6)	.285[a]
Neonatal birthweight (g)	3505 (3200–3850)	3500 (3160–3845)	3500 (3160–3860)	3480 (3120–3800)	3495 (3155–3880)	3505 (3168–3850)	3510 (3160–3860)	3505 (3175–3850)	3500 (3174–3830)	3460 (3115–3800)	3455 (3119–3780)	3465 (3140–3805)	3475 (3150–3800)	3470 (3145–3825)	<.001[b]

Continuous variables are illustrated as nonparametric data: median (interquartile range); dichotomous variables are presented as: n (%).

[a] χ^2 test for trend; [b] Kruskal-Wallis for trend analysis with the Jonckheere-Terpstra test for nonparametric data.

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Obstetric interventions

A total of 2983 fetal blood samples were performed in 2201 women (11.2%). Between 2000 and 2013 there was a significant reduction in the number of fetal blood samples, from approximately 11.8% to 8.8% (Table 3, Figure 1, A).

After adjustment for possible confounders (meconium-stained amniotic fluid, epidural analgesia, oxytocin augmentation of labor, induction of labor, and total number of vaginal instrumental deliveries), there was a strong decline in fetal blood sampling rate, which reached statistical significance in 2009. The adjusted OR from 2013 compared to 2000 was 0.45 (95% CI 0.34−0.60) (Appendix, Supplemental Table 2).

There was a statistically significant reduction in the total number of vaginal instrumental deliveries, from approximately 13.8% to 10.3%. Cesarean and vaginal instrumental deliveries for fetal distress and the total number of cesarean deliveries remained the same (Table 3, Figure 1, B).

After adjustment of the data, the declining trend in the total number of cesarean deliveries over time was more evident, based on lower odds ratios and narrower confidence intervals. The decrease in vaginal instrumental deliveries was also stronger and was significant from 2006 forward. For cesarean deliveries the adjusted OR from 2013 vs 2000 was 0.62 (95% CI 0.50−0.77) and for instrumental vaginal deliveries it was 0.43 (95% CI 0.34−0.55) (Appendix, Supplemental Table 2).

Neonatal outcomes

The sampling rates and neonatal outcomes are shown in Table 4. Umbilical cord blood data were obtained in 18,192 (92.5%) women. After 2001, the sampling rate was >90%. There were 1265 (7.0%) samples with an arteriovenous pH difference < 0.03 units and 3830 (21.1%); newborns had only a single umbilical cord sample.

The incidence of umbilical artery metabolic acidosis decreased significantly, from approximately 2.5% to 0.4%, which is a reduction of 84%. As shown in Figure 1, C, this decrease started with the beginning of the randomized trial in 2006. Umbilical artery acidosis also declined significantly, from approximately 1.3% to 0.4%.

The reduction in umbilical artery metabolic acidosis remained significant after adjustment for possible confounders, but the effect size was slightly reduced, with marginally broader confidence intervals. Starting in 2008, the decline became significant compared to the reference year 2000. In 2013 the adjusted OR for umbilical artery metabolic acidosis was 0.14 (95% CI 0.04−0.47). The decrease in umbilical artery acidosis was no longer significant after adjustment. (Appendix, Supplemental Table 3).

There were no significant changes with time for Apgar scores < 4 at 1 minute and Apgar scores < 7 at 5 minutes (Table 4).

Fourteen cases of moderate neonatal encephalopathy and 10 cases of severe neonatal encephalopathy occurred. Eight perinatal deaths occurred. The incidence of moderate and severe neonatal encephalopathy was 1.56 per 1000 births in the years 2000−2007 and 0.86 in 2008−2013, with an OR of 0.39 (χ^2; 95% CI 0.17−0.89; $P = .035$). One case with severe and 4 with moderate neonatal encephalopathy did not have umbilical artery metabolic acidosis, but did exhibit mild umbilical cord blood acidosis (pH <7.20).

Comment

Principal findings

Over a 14-year period during which ST waveform analysis methodology was implemented, we found an 84% reduction in the incidence of umbilical artery metabolic acidosis in neonates of 19,664 medium- and high-risk pregnant women. The rate declined from approximately 2.5% to 0.4%. Furthermore, there was a significant reduction in fetal blood sampling, cesarean deliveries, and vaginal instrumental

TABLE 3
Obstetric interventions: fetal blood sampling rates and delivery outcomes

Year	Deliveries, n	Fetal blood sampling rate, %	Cesarean delivery rate, %		Instrumental delivery rate, %	
			For fetal distress	Total	For fetal distress	Total
2000	1295	9.4	2.6	17.2	5.5	14.2
2001	1221	12.0	2.5	14.1	6.6	13.6
2002	1184	14.0	3.1	12.2	6.8	13.7
2003	1278	10.6	2.2	9.4	6.6	13.6
2004	1426	15.8	3.6	12.3	5.1	11.6
2005	1341	16.2	3.9	12.6	6.3	12.8
2006	1315	11.6	4.3	12.8	5.9	11.5
2007	1197	13.8	3.1	11.2	5.4	12.3
2008	1288	12.3	2.1	11.3	5.6	9.9
2009	1498	8.8	3.7	11.9	5.5	12.4
2010	1699	8.5	3.4	12.5	7.7	13.7
2011	1691	10.8	3.3	12.2	6.7	11.1
2012	1653	9.1	2.5	11.7	5.5	10.7
2013	1565	6.5	3.0	13.1	4.7	9.1
P[a]		<.001	.674	.185	.525	<.001

[a] χ^2 test for trend.

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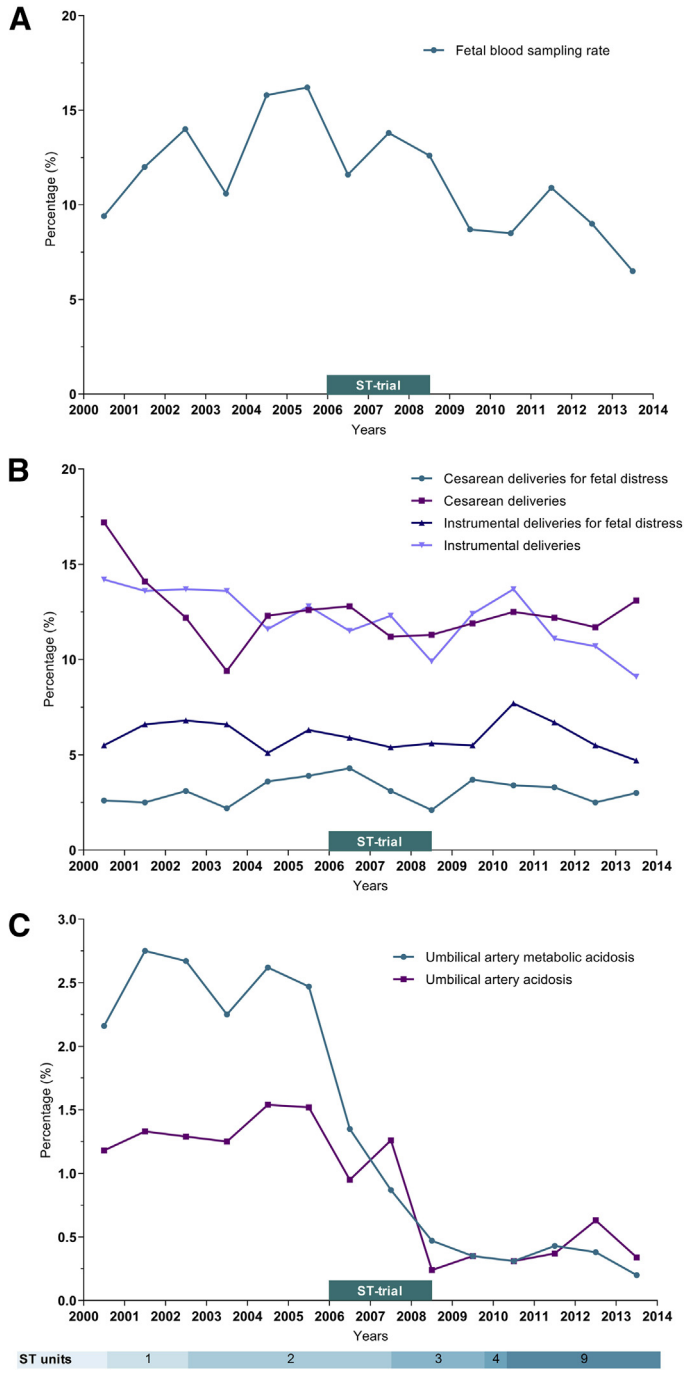
FIGURE 1
Perinatal outcomes between 2000 and 2013



A, Fetal blood sampling rates; **B,** Delivery outcomes expressed as percentages of cesarean deliveries for fetal distress, total number of cesarean deliveries, vaginal instrumental deliveries for fetal distress, and total vaginal instrumental deliveries; **C,** Incidence of umbilical artery metabolic acidosis (pH $<$ 7.05 and base deficit in the extracellular fluid $>$ 12 mmol/L) and umbilical artery acidosis (pH $<$ 7.00). Usage of fetal electrocardiogram ST waveform analysis, expressed as the number of monitors, is depicted under the graphs.

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deliveries. It is striking that the reduction in umbilical artery metabolic acidosis occurred during the period of the randomized trial, when only 20−25% of all women in labor were monitored with CTG+ST waveform analysis. Thereafter, the incidence of acidosis did not decrease any further, despite the increasing use of ST technology to nearly 100% by 2010. There was a significant reduction in the incidence of neonatal encephalopathy when comparing the years before and after the randomized trial.

Interpretation

The continuing decrease in umbilical artery metabolic acidosis rate in the years following implementation of ST waveform analysis—with increasing use of the technique as well as increasing experience of personnel—is in line with other studies with a similar design.[32,33,38,41] While these studies showed a gradual decrease in the incidence of umbilical artery metabolic acidosis over time, the incidence in our study did not decline parallel to the increasing use of ST waveform analysis. Rather, the greatest share of the decrease in umbilical artery metabolic acidosis took place in the period from 2006 to 2008 (80% between 2005 and 2008; from 2.47% to 0.48%). The incidence rate subsequently remained low.

The Dutch trial showed a nonsignificant 30% lower incidence of umbilical artery metabolic acidosis in the arm testing ST waveform analysis.[19,20] The present study demonstrates that the overall decrease in umbilical artery metabolic acidosis rate during this period was much larger. This implies that ST waveform analysis technology alone cannot have resulted in the observed decrease in acidosis and that other factors associated with its implementation must also have contributed, leading to improved outcomes of the CTG-monitored deliveries through crossover effects.[50] This can be explained by the intensified training of obstetric personnel in line with the clinical guidelines of ST waveform analysis, which also focused considerably on the classification and interpretation of CTG.

TABLE 4
Neonatal outcomes

Year	Deliveries, n	Umbilical cord sampling rate, %	Single vessel sampling, %	Umbilical artery metabolic acidosis,[a] %	Umbilical artery acidosis, %	Apgar scores <4 at 1 minute, %	Apgar scores <7 at 5 minutes, %
2000	1295	78.6	20.3	2.16	1.18	0.8	0.8
2001	1221	80.3	19.1	2.75	1.33	1.2	1.6
2002	1184	91.9	18.2	2.67	1.29	1.7	1.4
2003	1278	94.1	17.4	2.25	1.25	1.5	1.6
2004	1426	91.2	20.1	2.62	1.54	1.2	1.7
2005	1341	93.4	19.5	2.47	1.52	1.9	1.2
2006	1315	96.1	22.5	1.34	0.95	1.4	1.0
2007	1197	95.8	19.0	0.87	1.39	0.9	0.5
2008	1288	93.9	19.2	0.48	0.24	1.1	1.4
2009	1498	95.1	20.7	0.35	0.35	0.9	1.4
2010	1699	94.1	19.4	0.31	0.31	1.2	1.6
2011	1691	96.2	17.9	0.43	0.37	1.4	1.2
2012	1653	95.4	19.3	0.44	0.63	1.4	1.6
2013	1565	95.2	20.2	0.20	0.34	0.7	1.0
P[b]				<.001	<.001	.325	.888

The rates of umbilical artery metabolic acidosis and arterial pH <7.00 were calculated using the cases with available umbilical cord acid-base data, but using the total number of deliveries as the denominator did not have any consequences for the level of significance.

[a] Defined as pH < 7.05 and base deficit in the extracellular fluid > 12 mmol/L; [b] χ^2 test for trend.

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The effects of the Dutch trial itself could also have contributed to the major reduction in umbilical artery metabolic acidosis through the Hawthorne effect. The Hawthorne effect concerns all effects that are a consequence of research participation—thus being observed constantly—which are non-intervention-related and might impact behavior of both participants and medical personnel. This leads to improved results in both study arms of randomized trials owing to non-treatment-related factors such as increased clinical surveillance and more attention to adherence to clinical guidelines.[51] The Hawthorne effect is difficult to quantify, but, together with improved outcomes in CTG-monitored labors, it might have influenced the absence of a significant reduction in the incidence of umbilical artery metabolic acidosis in favor of the ST waveform analysis arm in several randomized trials.

Moreover, many randomized trials were underpowered to show a significant change in umbilical artery metabolic acidosis because the incidence of metabolic acidosis was lower than anticipated, which is probably partially attributable to improved perinatal outcomes in both study arms.[15–17,19–21] Similar trends were observed in other randomized trials assessing intrapartum fetal heart rate monitoring.[52,53]

Education and the learning curve following implementation of new technology might also explain conflicting results in different study designs. The presence of a learning curve is strongly supported by the Swedish randomized trial, which has shown significantly improved results in its second half.[15,16] This learning curve can mask a significant effect in a randomized trial. Furthermore, several observational studies also demonstrate a learning curve through a continuing decrease in umbilical artery metabolic acidosis rate.[32,33,38,41]

Continuous training and the discussion of cases in an audit setting reduced the number of protocol violations.[54] Still, the human role remains the limiting factor in fetal surveillance owing to misclassification of CTG, (unrecognized) poor signal quality of ST waveform analysis, and failure to adhere to the clinical guidelines.[55–58] However, the addition of ST waveform analysis to CTG does seem to have improved agreement regarding when to intervene, when not to intervene, and the timing of intervention.[59–65]

Research implications

Although randomized controlled trials represent the highest level of evidence, they do not always reflect daily clinical practice. Results may be influenced by the Hawthorne effect, but also by factors such as technical complexity, operator training, the learning curve, and even factors independent of the technology itself, eg, the experience and decision making of the acting clinicians.[66,67] This matter has been addressed in detail in other studies.[67,68] Real-world evidence,

ie, monitoring of outcome before, during, and after the introduction of new technology, may well give additional insight into its clinical value.[42] In this respect, it would be interesting to know the trends with time before, during, and after the US randomized trial, especially since the rate of the primary outcome was very low.

Strengths and limitations

A strength of our study is that it is a large cohort of deliveries with detailed information on perinatal outcomes and few missing data. However, there are some limitations of this study that need to be addressed.

First, an important shortcoming is that no record was kept of which deliveries were monitored with ST waveform analysis. Therefore, a definite causal relationship between ST waveform analysis and the observed results cannot be determined. However, a reduction of this magnitude during the short period of the randomized trial cannot be explained by continuing health care improvement strategies alone. It rather indicates that the randomized trial itself and implementation of the ST waveform analysis methodology must have contributed, as this was the only major intervention at our labor ward directly aiming to improve the identification of intrapartum fetal hypoxia and thus neonatal outcome. We do not believe simultaneous maternal heart rate monitoring could have significantly altered the results because internal fetal heart rate monitoring was applied.

Second, significant changes in the study population occurred during the study, which may have altered the risk of adverse outcome. Although results were adjusted for possible confounders, there might be confounders that we were not aware of or that were not recorded, eg, body mass index and smoking. However, we consider it unlikely that changes in the population may have altered the risk importantly. Moreover, the characteristics of the study population did not change between 2006 and 2008 when the greatest decline in umbilical artery metabolic acidosis occurred.

The third limitation is the retrospective nature of the study, which has implications for data collection. However, after data extraction all cases with missing data were manually reviewed and completed. Still, umbilical cord acid-base data were not obtained in 7.5% of the samples, and 20.1% were of venous origin, which implies that cases of umbilical artery metabolic acidosis may have been missed. However, this potential error was reduced by reviewing all Neonatal Intensive Care Unit admissions for cases with unfavorable outcome that were possibly related to asphyxia. Moreover, missing data may have reduced the effect on our observed decline in umbilical artery metabolic acidosis, taking into account that missing umbilical cord samples decreased during the study.

Conclusion

Implementation of ST waveform analysis of the fetal ECG has improved the outcomes of both CTG- and ST-monitored deliveries. We observed an 84% decrease in umbilical artery metabolic acidosis associated with participation in the Dutch randomized controlled trial. This is presumably largely attributable to several factors in addition to ST technology itself, eg, training according to ST clinical guidelines and the Hawthorne effect. Real-world observations differ from those obtained by randomized trials. ■

Acknowledgments

The authors would like to thank Marijke Doeve for extracting the data from our digital obstetric patient registration systems. Peter Zuithoff from Julius Support gave valuable advice regarding longitudinal statistical analysis and we are grateful for that.

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Received May 14, 2018; revised Jan. 17, 2019; accepted Feb. 22, 2019.

The authors report no conflict of interest. No funding was received for the preparation or the conduct of this research.

An oral presentation was given on the XXV European Congress on Perinatal Medicine 2016 (ECPM) in Maastricht, the Netherlands.

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SUPPLEMENTAL TABLE 1
Classification of neonatal encephalopathy by Sarnat and Sarnat[49]

	Mild (stage I)	Moderate (stage II)	Severe (stage III)
Level of consciousness	Hyperalert	Lethargic or obtuned	Coma
Muscle tone	Normal	Mild hypotonia	Flaccid
Seizures	None	Frequent (focal or multifocal)	Uncommon (excluding decerebration)
Complex reflexes	Weak	Weak or absent	Absent
Autonomic function	Generalized sympathetic	Generalized parasympathetic	Both systems depressed
Electroencephalogram findings	Normal	Early: low-voltage continuous delta and theta Late: periodic pattern	Early: periodic pattern with isopotential phases Later: totally isopotential
Duration	Less than 24 hours	2—14 days	Hours to weeks

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SUPPLEMENTAL TABLE 2
Obstetric outcomes analyzed using Generalized Estimating Equations with logistic regression

	Fetal blood sampling			Total cesarean deliveries			Total vaginal instrumental deliveries		
	Unadjusted		Adjusted	Unadjusted		Adjusted	Unadjusted		Adjusted
Year	%	OR (95% CI)	OR (95% CI)	%	OR (95% CI)	OR (95% CI)	%	OR (95% CI)	OR (95% CI)
2000[a]	9.4			17.2			14.2		
2001	12.0	1.32 (1.02–1.70)	1.37 (1.05–1.78)	14.1	0.82 (0.65–1.03)	0.83 (0.66–1.05)	13.6	0.95 (0.76–1.19)	0.95 (0.76–1.19)
2002	14.0	1.57 (1.22–2.01)[c]	1.62 (1.25–2.10)[c]	12.2	0.76 (0.60–0.97)[b]	0.77 (0.61–0.96)[b]	13.7	0.96 (0.76–1.20)	0.94 (0.75–1.18)
2003	10.6	1.14 (0.88–1.47)	1.15 (0.88–1.50)	9.4	0.58 (0.45–0.74)[c]	0.59 (0.46–0.74)[c]	13.6	0.95 (0.76–1.19)	0.90 (0.72–1.13)
2004	15.8	1.80 (1.43–2.28)[c]	1.90 (1.49–2.42)[c]	12.3	0.78 (0.63–0.98)[b]	0.74 (0.59–0.93)[b]	11.6	0.80 (0.64–0.996)[b]	0.74 (0.59–0.93)[b]
2005	16.2	1.86 (1.47–2.35)[c]	1.82 (1.42–2.33)[c]	12.6	0.83 (0.66–1.04)	0.80 (0.64–0.99)[b]	12.8	0.88 (0.71–1.10)	0.84 (0.67–1.05)
2006	11.6	1.26 (0.98–1.62)	1.14 (0.88–1.50)	12.8	0.85 (0.68–1.06)	0.74 (0.59–0.92)[c]	11.5	0.78 (0.62–0.99)[b]	0.71 (0.57–0.90)[b]
2007	13.8	1.54 (1.20–1.97)[b]	1.40 (1.08–1.81)[b]	11.2	0.72 (0.57–0.92)[b]	0.63 (0.50–0.80)[c]	12.3	0.85 (0.67–1.07)	0.76 (0.60–0.96)[b]
2008	12.3	1.35 (1.05–1.73)[b]	1.17 (0.90–1.52)	11.3	0.76 (0.60–0.96)[b]	0.62 (0.50–0.77)[c]	9.9	0.68 (0.53–0.86)[b]	0.58 (0.46–0.74)[c]
2009	8.8	0.92 (0.71–1.19)	0.61 (0.46–0.80)[c]	11.9	0.83 (0.66–1.03)	0.58 (0.47–0.73)[c]	12.4	0.86 (0.69–1.07)	0.65 (0.52–0.81)[c]
2010	8.5	0.90 (0.70–1.16)	0.55 (0.42–0.71)[c]	12.5	0.86 (0.70–1.07)	0.61 (0.49–0.75)[c]	13.7	0.96 (0.78–1.18)	0.73 (0.59–0.90)[b]
2011	10.8	1.17 (0.92–1.49)	0.78 (0.60–1.00)	12.2	0.85 (0.69–1.05)	0.57 (0.46–0.71)[c]	11.1	0.76 (0.61–0.94)[b]	0.57 (0.45–0.71)[c]
2012	9.1	0.96 (0.75–1.24)	0.64 (0.49–0.84)[b]	11.7	0.89 (0.72–1.10)	0.62 (0.50–0.76)[c]	10.7	0.72 (0.68–0.90)[b]	0.52 (0.42–0.66)[c]
2013	6.5	0.67 (0.51–0.88)[b]	0.45 (0.34–0.60)[c]	13.1	0.92 (0.74–1.14)	0.62 (0.50–0.77)[c]	9.1	0.60 (0.48–0.76)[c]	0.43 (0.34–0.55)[c]

Data are adjusted for meconium-stained amniotic fluid, epidural analgesia, oxytocin-augmentation of labor, induction of labor and total number of vaginal instrumental deliveries

CI, confidence interval; *OR*, odds ratio.

[a] Reference year for the calculation of odds and 95% confidence intervals for the consecutive years; [b] IP $< .05$; [c] $P < .001$.

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SUPPLEMENTAL TABLE 3

Neonatal outcomes analyzed using Generalized Estimating Equations with logistic regression

	Umbilical artery metabolic acidosis			Umbilical artery acidosis		
	Unadjusted		Adjusted	Unadjusted		Adjusted
Year	%	OR (95% CI)	OR (95% CI)	%	OR (95% CI)	OR (95% CI)
2000[a]	2.16			1.18		
2001	2.75	1.28 (0.73–2.27)	1.29 (0.73–2.31)	1.33	1.13 (0.51–2.48)	1.15 (0.52–2.55)
2002	2.67	1.24 (0.71–2.17)	1.31 (0.74–2.32)	1.29	1.09 (0.50–2.38)	1.17 (0.53–2.57)
2003	2.25	1.04 (0.59–1.84)	1.15 (0.64–2.14)	1.25	1.06 (0.49–1.27)	1.19 (0.55–2.58)
2004	2.62	1.22 (0.71–2.09)	1.37 (0.79–2.39)	1.54	1.31 (0.64–2.69)	1.54 (0.74–3.22)
2005	2.47	1.15 (0.66–2.00)	1.25 (0.71–2.21)	1.52	1.29 (0.62–2.67)	1.46 (0.70–3.08)
2006	1.34	0.62 (0.33–1.17)	0.72 (0.38–1.38)	0.95	0.80 (0.36–1.80)	1.00 (0.44–1.26)
2007	0.87	0.40 (0.19–0.85)[b]	0.47 (0.22–1.00)	1.39	1.19 (0.56–2.52)	1.47 (0.68–3.18)
2008	0.48	0.22 (0.09–0.55)[c]	0.29 (0.11–0.72)[b]	0.24	0.20 (0.06–0.72)[b]	0.27 (0.08–0.99)[b]
2009	0.35	0.16 (0.06–0.42)[c]	0.21 (0.08–0.58)[b]	0.35	0.30 (0.10–0.84)[b]	0.42 (0.14–1.25)
2010	0.31	0.14 (0.05–0.38)[c]	0.19 (0.07–0.51)[b]	0.31	0.26 (0.09–0.75)[b]	0.37 (0.13–1.07)
2011	0.43	0.20 (0.08–0.46)[c]	0.28 (0.11–0.69)[b]	0.37	0.31 (0.12–0.83)[b]	0.48 (0.17–1.33)
2012	0.44	0.20 (0.09–0.48)[c]	0.28 (0.12–0.68)[b]	0.63	0.54 (0.23–1.24)	0.81 (0.34–1.95)
2013	0.20	0.09 (0.03–0.31)[c]	0.14 (0.04–0.47)[b]	0.34	0.29 (0.10–0.81)[b]	0.47 (0.16–1.38)

Data are adjusted for meconium-stained amniotic fluid, epidural analgesia, oxytocin-augmentation of labor, induction of labor and total number of vaginal instrumental deliveries.

CI, confidence interval; *OR*, odds ratio.

[a] Reference year for the calculation of odds and 95% confidence intervals for the consecutive years; [b] $P < .05$; [c] $P < .001$.

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