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The "Fetal Reserve Index": Re-Engineering the Interpretation and Responses to Fetal Heart Rate Patterns

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Electronic fetal monitoring · Fetal Reserve Index · Neonatal encephalopathy · Cerebral palsy · ACOG monitoring classification system · Intrauterine resuscitation

Abstract

Objective: Electronic fetal monitoring (EFM) correlates poorly with neonatal outcome. We present a new metric: the "Fetal Reserve Index" (FRI), formally incorporating EFM with maternal, obstetrical, fetal risk factors, and excessive uterine activity for assessment of risk for cerebral palsy (CP). ***Methods:*** We performed a retrospective, case-control series of 50 term CP cases with apparent intrapartum neurological injury and 200 controls. All were deemed neurologically normal on admission. We compared the FRI against ACOG Category (I–III) system and long-term outcome parameters against ACOG monograph (NEACP) requirements for labor-induced fetal neurological injury. ***Results:*** Abnormal FRI's identified 100% of CP cases and did so hours before injury. ACOG Category III identified only 44% and much later. Retrospective ACOG monograph criteria were found in at most 30% of intrapartum-acquired CP patients; only 27% had umbilical or neonatal pH <7.0. ***Conclusions:*** In this initial, retrospective trial, an abnormal FRI identified all cases of labor-related neurological injury more reliably and earlier than Category III, which may allow fetal therapy by intrauterine resuscitation. The combination of traditional EFM with maternal, obstetrical, and fetal risk factors creating the FRI performed much better as a screening test than EFM alone. Our quantified screening system needs further evaluation in prospective trials.

Introduction

Electronic fetal monitoring (EFM) appeared as a clinical device for routine patient care beginning in 1969 and has become the primary means of intrapartum fetal surveillance throughout the world [1, 2]. Despite obvious beneficial impacts on intrapartum stillbirth, neonatal death rates, and reduction in neonatal seizures [3], EFM has failed to produce the expected reduction in long-term handicap rates including cerebral palsy (CP) [4]. With high rates of both intra- and interobserver error, it has been further criticized as an imprecise, subjective, and poorly predictive measure of fetal well-being with a high false positive rate and thus a poor screening test [5]. The poor screening performance metrics lead to unnecessary interventions [6] that also lack the discriminatory power to identify the truly hypoxic or injured fetus [7, 8].

There have been numerous attempts to standardize interpretation and management with new classifications continuing to appear that rely solely on the assessment of

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EFM parameters in predicting fetal acidemia [9–14]. Reliability has proven elusive, with deficiencies in identifying material endpoints and no apparent improvement in neurological outcome or reduction in allegations of obstetrical negligence [15–18]. Concomitantly, there are worldwide, controversial efforts to reduce the cesarean section rate in part by increasing the tolerance for increasing lengths of labor and for abnormal FHR patterns [19–21].

The premise of EFM is the recognition of fetal asphyxia related to metabolic acidemia. The response to FHR patterns is predicated on the identification and "rescue" of the hypoxic fetus hopefully before it has suffered damage. ACOG guidelines describe Categories I–III and are based exclusively on presumed degree of metabolic acidemia with intervention reserved for Category III [22]. Other publications, including the ACOG NEACP Monograph [23], demand fastidious criteria to attribute subsequent injury to intrapartum events, while others question appropriateness of Cesarean section for fetal indication without corroborating asphyxia [24]. We believe that a key problem in much of the literature is the mixing of CP cases that came into labor with evidence of damage already having occurred (e.g., biophysical profile score of 2, ultrasound determinable abnormalities, or clearly abnormal tracings on admission) as opposed to those cases in which there is no evidence at the time of admission of any concern [25]. In this study, we include only CP patients delivered at term, who, at the time of admission, showed no evidence of abnormality and for whom subsequent evaluation provided unequivocal evidence of injury during labor.

Here, we combined the traditional EFM parameters (fetal heart rate baseline rate, variability, accelerations, and decelerations) with clinical risk factors and excessive uterine activity (EXUA) to create an improved, quantifiable, on-going "screening" test for normal fetuses from the outset of labor to allow earlier accurate identification of developing risk. Earlier recognition of high risk would allow fetal therapeutic measures (intrauterine resuscitation [IR] or expedited delivery) to be instituted with the goal of improving the outcome of fetuses at risk for intrapartum neurological injury. Despite previous attempts to develop a risk stratification model to predict or enhance adverse neonatal outcome (low pH, low Apgar score, and NICU admission in labor) [15, 26], to our knowledge this combined scheme has not been attempted previously in demonstrably normal fetuses for whom neurological handicap was reasonably demonstrated to have been acquired during labor.

Methods and Materials

This risk scoring system formally includes both antepartum and intrapartum risk factors that contribute to adverse neurological outcome in the newborn. Our conceptual notion is that interpretation of FHR should be optimized, not for the recognition of asphyxia or "rescue," but for the prevention of injury. We define a new term, the "Fetal Reserve Index" (FRI), which is a weighted calculation of various maternal, fetal, and obstetrical risk factors (MOFR) along with FHR interpretation and EXUA. This study compares the FRI against the current ACOG classifications (ACOG Category III and ACOG monograph NEACP criteria) in a case-control model.

The study cases derive from 50 medico-legal consultations of one of the authors (B.S.S.) in babies subsequently shown to have neurological handicap. They come from diverse geographical and institutional settings in the United States ranging from small community hospitals to large metropolitan, university-affiliated, and resident intensive obstetrical programs. The deliveries occurred between 2000 and 2013. All study patients were deemed to be at term (>36 weeks) with singleton pregnancies in vertex presentation who, irrespective of any maternal complications, presented for a trial of labor with normal FHR patterns and no evidence of prior neurological injury or anomaly. The fetal admission test developed by Phelan in the 1990s demonstrated that a fetus with a normal baseline rate, normal variability, absent late decelerations, and a reactive NST essentially rules out any significant neurological injury associated with hypoxia/asphyxia [27]. The literature is replete with numerous publications dating back to the 1970s concluding that a reactive fetus is neurologically intact with respect to hypoxia/asphyxia injury [28–30].

Elective cesarean sections, anomalous fetuses, and those with known abnormalities (even if only in retrospect) were excluded from both study and control groups. In all study cases, the diagnosis of long-term injury (CP) was confirmed by neurological and neuroradiological examinations in the perinatal period with a minimum of 2-year follow-up. Despite the date of case accumulation, retrospective evaluations were performed for the study from original data in the past year using current, accepted methods of interpretation of factors such as monitor interpretation and categorization of risk factors.

Given the nature of the retrospective study group, there is no perfect control group readily available. Our control group consisted of consecutive cases from the obstetrical service of one of the authors (R.D.E.) undergoing a trial of labor (≥34 weeks) for whom FHR tracings on admission were also deemed normal and reactive. Because the CP cases came from multiple locations, there was no way to match the controls to them individually other than the presence of normal fetal tracing on admission in a patient undergoing a trial of labor at term. Because they are poor predictors of fetal neurological injuries during labor, there were no exclusions in either group for antenatal risk factors (hypertension, diabetes, etc.), parity, route, timing, or urgency of delivery. Demographic, EFM and clinical maternal, obstetrical, fetal, and neonatal variables were de-identified for the analysis and as such qualified for exemption as evaluated by the Biomedical Research Association of NY IRB. (#16-12-180-429). There was no outside funding and no conflicts of interest related to such. One of us (M.I.E.) has obtained a US Patent for the scoring system (US Patent 9,131,860 with others pending).

Patient data were categorized as demographic and clinical during the antepartum and intrapartum periods. As per inclusion criteria, all fetuses had normal head size at the time of birth. Variables analyzed included standard demographics, medical, obstetrical, and fetal risk factors. The vast majority of these risk factors have been well studied and known to be associated with adverse perinatal outcome for over 4 decades. We adopted these well-vetted risk factors from standard texts and literature. In fact, they serve as the basis of the Hollister and ACOG prenatal forms that in part were devised by a landmark contribution by Hobel et al. [31] in the 1970s who emphasized the importance of risk stratification for both antepartum and intrapartum periods [32]. Medical variables included gestational disorders (hypertension, diabetes, maternal age, BMI >40, and nulliparity) and chronic medical disorders, e.g. collagen, respiratory or cardiac. These are clearly associated with an unmeasured risk of adverse outcomes but are not included in EFM interpretation. Obstetrical variables included parity, gestational age, need for induction of labor, use of oxytocin and/or prostaglandin, duration of labor (by stage), and type and urgency of delivery. Fetal factors included abnormal Dopplers/biophysical profile, evidence of growth or genetic disorders, meconium, etc. (Table 1).

Neonatal Assessment and Follow-Up

Neonatal variables included standard outcome data such as birth weight, Apgar scores at 1, 5, and 10 min (when appropriate), head circumference, umbilical and neonatal pH and blood gases, neonatal adaptation, seizures, and length of stay. For cases, follow-up examinations beyond the neonatal period included type of CP, the presence of microcephaly, hemiplegia, mental retardation, and developmental delay and seizures. Cardiac, respiratory and neurological events (seizures/coma) were recorded whether or not the newborn received cooling for neuroprotection. Acidosis was defined as per ACOG criteria as a pH <7.0/BD ≥12 mEq/L in either umbilical or neonatal blood. Neonatal imaging study results were evaluated by technique (ultrasound, MRI, CAT scan) as well as the type and location of the lesions (cortical – white or gray matter, basal ganglia, stroke, other) and their symmetry. The diagnosis of hypoxic-ischemic encephalopathy (HIE) was derived from the neonatal record and related to clinical and neuroradiological findings including recent HIE (prolonged, partial, or acute), hemorrhage, and "stroke."

In this report, however, we have subdivided the cases according to the severity of both the acidosis, umbilical, and neonatal impairment [33]. Long-term outcomes were assessed in terms of developmental delay, microcephaly, mental retardation, seizures, and problems of movement. Follow-up on study cases ranged from 2 to 16 years. We attempted to classify the type of CP (e.g., spastic quadriplegia, dyskinetic CP, and hemiplegia, but classification was not productive in that these diagnoses were not consistently used in the various follow-up examinations.

In this series, no follow-up examinations were deemed necessary or performed in the control group. Such is essentially standard throughout the literature. As with virtually all studies, normal outcomes in the control group were assumed if the control newborn was discharged in a timely way, with no evidence of residual disease and specifically no evidence of neonatal encephalopathy. Our exclusion concept of other causes of CP is exactly as stated in the original ACOG NEACP monograph as one of us (M.I.E.) articulated it for both works [23].

Table 1. Risk factors

Maternal risk factors

1 Decreased cardiac output/vascular perfusion of the placenta
   a Cardiac disease with risk of decreased cardiac output in pregnancy
   b Hypertension (chronic and pregnancy induced)
   c SLE, etc.
2 Oxygen carrying capacity
   a Pulmonary disorders (e.g., asthma)
   b Anemia and hemoglobinopathy
3 Infection (chronic and acute]
4 Chronic debilitating disease
5 Malabsorption/poor weight gain
6 Endocrine – diabetes and thyroid disorders
7 Advanced maternal age
8 Drug abuse, addiction, and smoking
9 Obesity – BMI >35
10 Short stature (≤5′2″)

Obstetrical risk factors

1 IUGR/macrosomia
2 Oligohydramnios
3 Polyhydramnios
4 Bleeding and abruption
5 Previous cesarean section
6 Placental and umbilical cord anomalies
7 Rupture of membranes (PPROM, SROM, AROM)
8 Dystocia (protraction and arrest disorders of labor)
9 Malpresentation

Fetal risk factors (demographic)

1 Abnormal Dopplers/BPP
2 Genetic disorders
3 Fetal arrhythmia
4 Meconium passage
5 Chorioamnionitis
6 Second stage of labor-pushing
7 Amnioinfusion
8 Discontinuation of pitocin due to fetal intolerance
9 Conversion patterns (acute prolonged tachycardia) (>170 bpm)
10 Ominous overshoots
11 Bradycardia (<100 bpm)
12 Missing important data in labor (e.g., lack of EFM in second stage)

Assessment of FHR and Uterine Contraction Patterns

The evolution of FHR and uterine contraction changes during labor were monitored from the outset of monitoring. The analysis of the FHR features was made according to standard American definitions for baseline heart rate, variability, decelerations, and accelerations as has been used for many years and in hundreds of publications (Table 2a). We have considered these as individual components, but the definitions of normality/abnormality are standard. Final baseline heart rate and variability immediately prior to delivery (e.g., bradycardia, tachycardia) were tabulated.

Table 2. Electronic fetal monitoring classification

a Features of fetal heart rate patterns

Fetal heart rate	
Basal rate	Normal, stable heart rate at the outset of monitoring
Baseline rate	Heart rate at any moment in time – averaged over 20 min – caveat
	Normal
	Rate between 110 and 160 bpm[a]
	Abnormal
	Baseline tachycardia[a] >160 bpm
	Baseline bradycardia[a] –<110 bpm
Baseline variability: variability assessed between uterine contractions and absent pushing	
Normal variability – >5 <25 bpm	
Abnormal variability	Decreased/absent FHR variability <5 bpm
	Sinusoidal, or nodal
	Increased FHR variability >25 bpm
Accelerations	
Normal	At least two FHR accelerations of >15 bpm (at peak) and 15 s duration (from onset to offset – associated with normal baseline variability and stable baseline rate)
Abnormal: abnormal – pathological	Overshoots – increase in baseline FHR rate following contractions associated with decreased variability and absence of "shoulders"
FHR decelerations	
Early/mild variable: either term suffices	Decelerations confined to the time period of the contraction
Variable decelerations: abrupt decelerations >30 bpm	
Late decelerations: any amplitude, but must be recurrent and proportion in amplitude and duration to the amplitude and duration of the underlying contractions	
Prolonged decelerations: deceleration lasts longer than 2 min	
Decelerations: "recovery"	
Normal	Each deceleration is modified by whether or not it has "recovered," i.e., it has returned promptly to the previously normal baseline rate and variability; this must be affirmatively demonstrated; it cannot be assumed, if there are technical issues
Abnormal (not recovered)	Prolonged overshoot >15 s
	Recovers to higher rate or increased variability
	Progressively rising rate until next contraction
	Slow return to the baseline
Conversion pattern: an abrupt alteration in baseline rate and/or variability – usually in association with ongoing variable decelerations or prolonged deceleration (see examples)	
Dropped data	
First stage of labor	With previously normal tracing – allow 20 min
	With previously abnormal tracing – immediate evaluation and possible intervention
2nd stage of labor	Failure to determine or establish a baseline rate *immediately* following deceleration ×2 is considered pathological; assigned to point A

[a] Duration of at least 10 min.

Two other variables were measured but not included in the FRI score: point "A" corresponds to that time in the tracing where the fetus is manifesting early deterioration (decompensation) and that intervention, but not necessarily delivery is called for (i.e., IR including discontinuation of oxytocin, cessation of pushing, or consideration of delivery with IV fluids and oxygen by mask) as one can no longer be certain of the health of the fetus in the context of the estimated feasibility of safe vaginal delivery. In many respects, point A corresponds to the "hypoxic criteria" for variable decelerations by Cibils [34], the "serious" criteria set forth by Clark et al. [10] in an algorithm for managing Category II patterns, and "subacute hypoxia" of Pinas and Chandraharan [35]. While all point As would be classified as ACOG Category II, only a small percentage of Category II qualified as point A. No attempt was made to determine any specific degree of fetal hypoxia or acidemia.

Table 2 (continued)

b Features of uterine activity

	Normal (20 min)	Abnormal
Frequency	≤8 contractions	>8 UC (tachysystole)
Duration	<90 s	>90 s
Increased tonus	With toco	Coupling/prolonged >120 s
	With IUPC	>20 mm Hg
Interval A	Interval – peak to peak	<2 min
Interval B	Interval – offset of UC to onset of next UC	<1 min
Rest time	>50%	<50%

Point "B" is the pattern seen after neurological damage to the fetus has occurred [36]. This pattern was identified – irrespective of Category (II–III) or perceived presence of fetal acidemia. Points A and B were determined blindly by one of the investigators (B.S.S.) who did not participate in the FRI risk scoring of the labor, tracings, or statistical analysis. All data and tracing evaluations for the study were done in the last year regardless of when the case actually occurred. While points A and B are the work of one of the authors, and reasonable experts might have slightly different conclusions, they were used in exactly the same fashion for all the statistical methods, so there should be no biases towards any method.

In assessing the course of labor and expectations of the feasibility for safe vaginal delivery and mindful of potential discrepancies in terminology [37], we have assigned risk factors according to perceived abnormalities of labor using the terminology for progress in labor proposed by Friedman (arrest and protraction disorders of cervical dilatation and descent) [38, 39].

Calculation of FRI

The FRI weights various MOFR according to their anticipated effect on maternal well-being, placental and cerebral perfusion, and the probability of safe vaginal delivery. The FRI was calculated for each 20 min segment of monitoring. In the calculation, each of 8 categories is assigned a "1" if the category was deemed normal and "0" if abnormal (Table 3). The MOFR variables are static, that is, once they occur, the reduction in point for each category remains until the fetus delivers. The EFM and EXUA variables, however, are dynamic and therefore may change as the characteristics of the FHR tracing change. The FRI was calculated on the number of points divided by 8 and multiplied by 100 to give a percentage. A total of 8 categories being normal would result in an FRI of 100 (8/8). A loss in points would result in an FRI of 87.5 (7/8), 75.0 (6/8), 62.5 (5/8), 50.0 (4/8), 37.5 (3/8), 25.0 (2/8), 12.5 (1/8), and 0 (0/8).

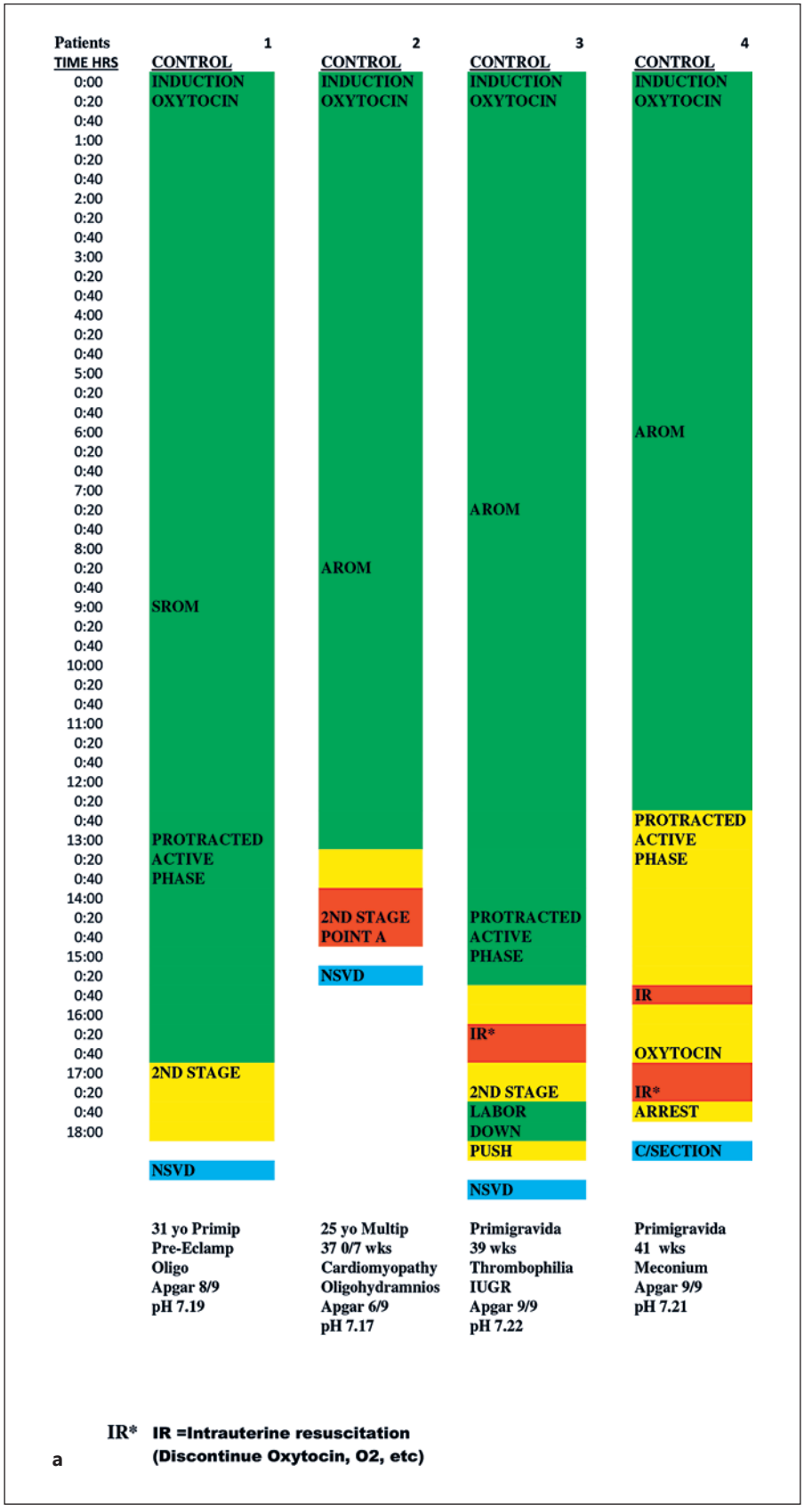
For the purposes of this study, an abnormal FRI was defined as 25 or less (corresponding to the "red zone" – see below). The calculation of the FRI as primary evaluation would, of course, be abandoned in the face of certain "sentinel" events – clinical maternal, fetal, and obstetrical events deemed to represent sufficient, immediate indication for intervention irrespective of the other features. These include, for example uterine rupture, umbilical cord prolapse, maternal hemorrhage, seizures, coronary compromise, and a persistent FHR bradycardia that persisted for >10 min – although no such examples were present in this series.

Table 3. Components of the fetal reserve index

1	Fetal heart rate
2	Baseline variability
3	Accelerations
4	Decelerations
5	Uterine activity
6	Maternal risk factors
7	Obstetrical risk factors
8	Fetal risk factors (separate from EFM)

Time intervals were calculated for length of labor, length of 2nd stage of labor, time of first onset of abnormal FHR characteristics to delivery, point A, point B, and presence of Category III tracing. In addition, the total time (based on 20 min segments) of each of the FHR characteristics was also analyzed. Finally, the lowest FRI score and its duration during labor, the last FRI score, and its appearance and duration of time during labor were determined.

As with many tests such as high school subjects, medical boards, and others, there is an official test score obtained (e.g., 80, 90, 100), which then also generates a "grade" given (e.g., A, B, C, pass, fail). For the FRI, we developed both a specific score (see above) and a grade for easy interpretation. For convenience, akin to traffic lights, arbitrary (color) zones were created for the FRI score and plotted consecutively for each of the 20-min segments. Normal (green zone) included FRI scores >50, Caution (yellow zone) included FRI scores ≤50 and >25, and Diligent ≤25 (red zone). Time intervals from the onset of yellow and red zone to points A, B, and delivery were also analyzed as was the total time (in 20-min segments) of each zone during the labor (Fig. 1). Direct comparisons among the FRI, Category III ACOG tracings, and ACOG Monograph criteria were also performed with the understanding that the FRI is dependent upon FHR/uterine contraction changes as well as clinical data. We are unaware of any other intrapartum risk classification that attempts to determine the timing of fetal injury, although ACOG affirms that injury may be inferred if the tracing goes from Category I to Category III [40]. Statistical analyses were performed with independent samples t tests, χ^2, and stepwise, logistic regression, and Levene's test for equality of variance analyses using SPSS software.



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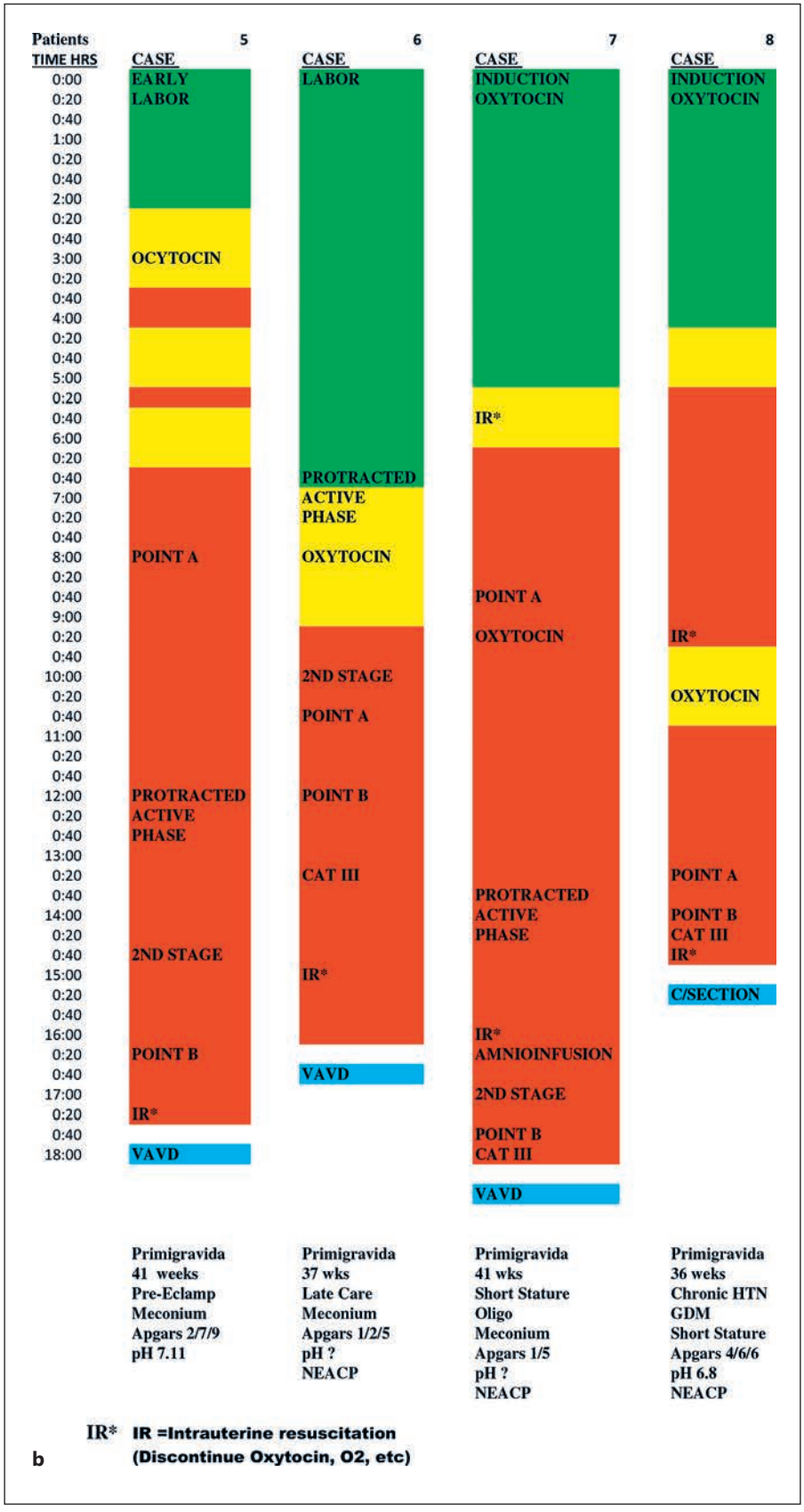

Fig. 1. a Four representative control patients. Each column is a different patient. Most of the time periods are scored in the green zone. Very little is in the red zone, and cases 3 and 4 show reversion of red to yellow following IR. **b** Four representative CP cases. Red zone is reached before the end of the first stage, and the patients remain in the red zone for several hours before delivery. In all 4 of these cases, red zone proceeds to points A and B. Category III is reached in 3 of the 4 which is a higher percentage than the overall series. In all 4 cases, the ACOG HIE criteria were not met (pH <7.00 and Apgar ≤3 at 5 min).

Table 4. Patient demographics and basic outcomes

	Cases	Control	*t*	χ^2	*p*
Maternal age, years	24.5±5.4	27.4±5.6	3.4		<0.001
Primip./multip.	38/12	79/121		21.4	<0.00001
GA, weeks	39.1±1.5	38.1±2.4	3.5		<0.001
Weight, g	3,438±556	3,065±598	3.99		<0.001
1-min Apgar	3.1±2.5	7.8±1.2	13.2		<0.001
5-min Apgar	5.4±2.8	8.9±0.5	8.7		<0.001
pH	7.05±0.19	7.2±0.06	4.3		<0.001
Labor, h	17.7±3.6	12.8±2.5	4.3		<0.001
Induction, y/n	38/12	93/107		14.0	<0.05
pH <7.00, y/n	8/23[a]	0/200		53.4	<0.0001
+ ACOG criteria, y/n	15/35	0/200		53.8	<0.00001
NEACP baby	50/0	0/200			

[a] Not available for 19 cases.

Results

There were some statistically significant demographic differences between cases and controls which we do not believe significantly impacted any of the main findings. The differences for FRI and outcomes between the study and control groups were so large to the point where any demographic differences could not reasonably be believed to explain any significant proportion of the variance (Table 4). These included maternal age, proportion of nulliparas, and birth weights for which study patients were younger and closer to term which if anything would be thought to lower risk, but they were also more likely to have been induced and have heavier maternal weight which can increase risk. Many patients in both groups had multiple maternal risk factors which have not been included in previous monitor tracing interpretation. Evaluation of the incidence of the risk factors between the cases and controls showed, not surprisingly that risk factors were more common in the case group. Combined, overall in the CP cases, there were an average of 4.38 risk factors/study patient versus 2.38 risk factors per control patient (NS). There were individual, significant differences such as for hypertension including pre-eclampsia (44 vs. 20%, $\chi^2 = 11.1$, $p < 0.001$), morbid obesity (20 vs. 4%, $\chi^2 = 15.3$, $p < 0.0001$), previous cesarean section (11 vs. 6%, $\chi^2 = 49.2$, $p < 0.0001$), and meconium (24 vs. 7.5%, $\chi^2 = 11.3$, $p < 0.001$). For most of the individual markers, the instances were low, limiting the power for statistical interpretation with this sample size. While sometimes suggestive, the numbers were too preliminary for substantive analysis.

Ultimately, whatever the maternal, fetal, or obstetrical risks prevailed in each of these patients, a trial of labor was taken under by their clinicians with the expectation of vaginal delivery of a neurologically normal baby. Levene's tests were noncontributory.

There were significant differences in the various measurements of the duration and rate of progress during labor (Table 4). The duration of both the 1st and 2nd stages of labor, the need for operative delivery, and the urgency of intervention were all greater in the case group. In addition, the indications for intervention commonly involved concern for the fetus.

As expected, many features of the fetal heart rate pattern were significantly different between study and control patients (Table 5). All study patients reached point A compared to 8.5% of the control group ($p < 0.001$). No control patient reached point B, while 48 of 50 (96%) study patients reached point B. Of the 2 study patients in whom the timing of point B could not be assessed, the final tracings were actually detecting maternal, not the fetal heart rate pattern (Table 6).

Both the use of oxytocin and the appearance of EXUA were ubiquitous in the study group and common in the control group ($p < 0.001$). Almost all cases of EXUA were associated with the use of prostaglandins and oxytocin. As with other investigators, diminished rest time between contractions correlated better with adverse outcome than did the frequency of contractions [41].

Cases had much lower 1-, 5-, and 10-min Apgar scores than controls ($p < 0.001$). Cord gases were available in the majority of cases and were obtained in 100% of our control population. The distribution of cord gas values in the

Table 5. Fetal reserve index results

	Cases	Controls	*t*	*p*
Lowest FRI score	15±4.1	40±28.1	18.79	<0.001
Hours lowest FRI	2.2±1.7	0.9±0.2	5.34	<0.001
Last lowest FRI	25.5±0.5	42.9±0.4	7.87	<0.001
Hours last FRI	2±1.6	0.9±1.6	4.29	<0.001
FRI at end stage 1	23±18.3	62±12.1	16.30	<0.001
2nd stage hours	2.9±1.6	1.0±0.8	11.20	<0.001
2nd stage 20-min segments	5.7±4.6	1.5±2.0	9.12	<0.001

Table 6. Fetal reserve index performance statistics

	Cases	Controls	χ^2	*p*
1st stage worst color			103.1	0.00001
Green	0	125		
Yellow	13	55		
Red	37	20		
2nd stage worst color			117.5	0.00001
Green	0	17		
Yellow	0	131		
Red	48	28		
Overall worst color			103.7	0.00001
Green	0	16		
Yellow	0	140		
Red	50	44		

study group showed that only about 30% had pH values at or below 7.0 (Table 4). None of the controls did. The vast majority of neuroradiological exams and reports describe white matter injury – so called partial, prolonged pattern involving either periventricular white matter and/or adjacent cortical gray matter injury; only about 8% had involvement of the basal ganglia, invariably in association with fetal bradycardia. About 1/3 had some evidence of intracranial or extracranial hemorrhage (the latter cases were confined to cases involving vacuum extraction). Over 80% of the fetuses suffered injury during the 2nd stage of labor, about 15% suffered injury in the latter part of the 1st stage, and 2 were injured in association with an attempted operative delivery. In these cases, the tracing reached point B only during the conduct of the vacuum or forceps. In the other 6 cases in which the vacuum was used, injury appeared during the 2nd stage of labor prior to the application of the device.

The FRI score was significantly lower in cases than controls both for lowest FRI, hours at the lowest FRI, and lowest FRI in the first stage ($p < 0.001$ for all; Table 5). The duration of lowest FRI scores was much longer in cases than controls (2.2 vs. 0.9 h) ($p < 0.001$) which also correlated with a much higher incidence of operative deliveries ($\chi^2 = 5.34$, $p < 0.001$).

FRI zones (green, yellow, red) were used to develop predictive statistics for adverse neonatal and long-term handicap. All study cases reached the red zone and remained there for an average of over 6 h before delivery. By the end of the 1st stage of labor, all study patients had reached the yellow zone, and 37 (74%) had reached the red zone. At the time of delivery, 47 (94%) of study patients exceeded 2 h in the red zone. The clinical course of the 1st and 2nd stages of labor, the response to the fetal therapy of IR, and the timing and route of delivery are graphically shown in Figure 1a, b. The graphs illustrate that cases had substantially more time in the red zone than controls (Fig. 1a). The typical pattern showed progression through the various zones (green, yellow, red), then reaching point A, and point B.

Conversely, 66% of the controls reached the yellow zone, and 22% reached the red zone. Of these, 37 and 10% reached the yellow and red zones, respectively, during the 1st stage of labor. Of those controls reaching the red zone, there was an average of 1.2-h duration before delivery versus 6.3 h for cases ($p < 0.001$). The 2nd stage seems to be a particular time of vulnerability for the fetus with as much as 80% of cases worsening significantly in the second stage (Tables 6, 7). In the study patients, there was no example of reversal (improvement) of color zone designation once the patient had entered the 2nd stage, which is in part a by-product of the algorithm as points are deducted for being in the 2nd stage. However, reversal of risk strata did occur in a few control patients (Fig. 1b).

The red zone appeared earlier in labor and more commonly in study patients than controls ($\chi^2 = 93.1$, $p < 0.00001$; Table 6). In addition, the time to reach point A was shorter in cases than controls. The time from yellow to delivery was much greater for cases than controls ($p < 0.001$). In the regression analysis, time in labor or either stage of labor were not independent predictors of injury. Likewise, time from entrance into the red zone to delivery was much greater for cases keeping in mind that only a minority of controls got to the red zone (22%), while 37/50 (74%) of cases reached the red zone in the 1st stage versus only 20/200 of the controls (10%) ($\chi^2 = 103.1$, $p < 0.00001$) (Table 6).

Table 8 lists the assessment of the individual components of the FRI by stepwise logistic regression; it shows that abnormal variability and red zone explained the highest proportion of the variance ($p < 0.001$) (Table 9).

Table 7. Time intervals

	Time, h		*t*	*p*	Cases	Controls	χ^2	*p*
	Cases	Controls						
Pt A to Del	4.0±2.4	0.6±0.4	5.96	0.0001	50/0	17/183	170.7	0.00001
Yellow to Del	10.8±4.6	2.4±3.3	11.92	0.001				
Pt B to Del	1.3±0.8	NA			48/2	0	237.6	0.00001
Pt A to Pt B	2.7±2.1	NA			48/2	0	237.6	0.00001
Red to Del	6.3±3.6	1.2±1.5	9.16	0.001				

Table 8. Time to points A and B

	Time to point A		t	*p*	Time to point B	
	cases	controls			cases	controls
ABN FHR	0.3±2.3	0.9±1.4	0.95	n.s.	3.1	n.a.
ABN VAR	6.1±4.4	0.8±1.8	6.81	<0.001	8.6	n.a.
Absent accel.	3.7±4.9	0.9±1.6	3.6	<0.001	6.2	n.a.
ABN decel.	4.8±4.7	3.2±3.1	1.28	n.s.	7.6	n.a.
XS UT activity	7.7±5.2	6.8±6.6	0.51	n.s.	10.4	n.a.
Yellow	6.9±4.5	3.6±3.8	2.68	<0.009	9.3	n.a.
Red	2.3±3.3	0.9±1.4	2.37	<0.02	5.1	n.a.

Discrimination in the 2nd stage and for the lowest FRI was even greater ($\chi^2 = 117.5$ and 103.7, both $p < 0.00001$) (Table 6).

Of the 50 cases of injury, only 8 (16%) satisfied the 2003 ACOG criteria for intrapartum injury. If we extrapolate from the available clinical and neonatal findings, we estimate that 15 cases would have met them had we had complete data (usually the pH values were missing). This would increase the sensitivity to 30%. For the FRI, all 50 were deemed to be injured (100%) ($\chi^2 = 53.8$, $p < 0.00001$) (Table 10). Since predictive values vary with prevalence, in studies such as this in which there is an artificially increased proportion of cases to controls, the positive predictive values (PPV) must be interpreted with great caution. The PPV of reaching the red zone in the first stage was 65%. The negative predictive value (NPV) was 93%. Performance in the second stage and overall was even better (PPV 63%, NPV 100%) (Table 10).

Evaluation of points A and B showed sensitivities the same as the FRI, and all were far higher than for both intrapartum assessment by ACOG criteria (prospective evaluation) and correlation with NEACP intrapartum injury (retrospective criteria). The PPV of the FRI was 53%, and A was 75%. Point B was predictive of neurological handicap in 100%. By that time, however, the damage was already done although detectable prenatally for B and analyzed postnatally for ACOG (Table 10). If only the newborn is considered, less than half of the cases would have met NEACP monograph criteria for intrapartum injury.

We performed a direct comparison between the FRI and ACOG category III for detection of abnormal outcomes. The FRI (reaching red zone) had a sensitivity of 100% (50/50), whereas Category III had a sensitivity of 44% (22/50) ($\chi^2 = 38.9$, $p < 0.00001$) (Table 10). At reaching point A, the average FRI was 16.5, reaching point B at 3.9. For the 22/50 CP cases that got to Category III, the FRI was for them 1.7, consistent with a bimodal population of the parameters producing Category III. For some cases, Category III could be very sensitive, but for others it is not (similar to the mixture model in nuchal translucency screening). This reduces its clinical utility as a screening test. The ACOG criteria would have only identified at most 30%, and Category III only 44% of these, whereas our system would have picked up all 50 (100%) as being at very high risk – and did so an average of 6.3 h before delivery, and we believe before irrevocable damage had been done. Controls who got to the red zone spent only 1 h there. Using our system, only 17 of 200 (8.5%)

Table 9. Timing of abnormalities

	Cases	Controls	*t*	*p*	EQ VAR
a *Time to delivery from 1st diagnosed abnormality*					
ABN FHR	4.5±3.2	1.2±1.3	6.25	<0.001	N
ABN variability	10.1±4.7	2.1±3.5	8.92	<0.001	N
Absent accel.	7.7±5.2	1.2±1.2	8.45	<0.001	N
ABN decel.	8.7±4.9	2.4±3.3	8.6	<0.001	N
XS uterine activity	11.8±5.3	4.8±4.7	8.78	<0.001	Y
Yellow	10.8±4.6	2.4±3.3	11.92	<0.001	N
Red	6.3±3.6	1.2±1.5	9.16	<0.001	N
b *Total hours with the abnormality*					
ABN FHR	2.8±2.0	0.2±0.5	9.18	<0.001	N
ABN variability	8.9±4.5	0.3±1.4	13.24	<0.001	N
Absent accel.	6.3±3.8	0.2±0.6	11.32	<0.001	N
ABN decel.	6.6±3.4	1.5±2.1	9.23	<0.001	N
XS uterine activity	9.9±5.4	3.2±3.7	8.28	<0.001	N
Yellow	5.2±3.5	1.8±2.6	6.48	<0.001	N
Red	5.4±2.9	0.2±2.6	12.63	<0.001	N
c *Ratio hours with ABN/time since 1st diagnosed abnormality*					
ABN FHR	0.75±0.10	0.14±0.03	11.23	<0.001	Y
ABN variability	0.90±0.08	0.14±0.02	20.9	<0.001	N
Absent accel.	0.89±0.11	0.17±0.02	19.22	<0.001	N
ABN decel.	0.85±0.12	0.82±0.12	0.58	n.s.	Y
XS uterine activity	0.84±0.15	0.74±0.10	2.06	n.s.	N
Yellow	0.50±0.19	0.87±0.14	3.47	<0.001	Y
Red	0.90±0.20	0.19±0.04	18.34	<0.001	N

Table 10. Screening performance of methods

	FRI[a]	Category III[a]	ACOG[b]	Point A[a]	Point B[a]
Cases/controls, *n*	50/200	50/200	50/200	50/200	50/200
Sensitivity	100 (50/0)	44 (22/28)	30 (15/35)	100 (50/0)	96 (48/2)
Specificity	78 (156/44)	78 (156/44)	100 (200/200)	92 (183/200)	100 (200/200)
Positive predictive value[c]	53 (50/44)	33 (22/44)	100 (15/15)	75 (50/67)	100 (48/48
Negative predictive value[c]	100 (156/156)	85 (156/184)	85 (200/235)	100 (183/183)	99 (200/202)

[a] Prospective data. [b] Retrospective data. [c] Must be interpreted with great caution.

controls ever got to point A, and none to point B. Of 50 NEACP cases, 48 got to point B and on average 1.3 h prior to delivery.

Discussion

This is the first study using the FRI, which incorporates MOFR, EXUA, and EFM in a scoring system modified to assess fetal perfusion and resilience rather than "hypoxia." MOFR, EXUA, and the specific identification of injury from the FHR pattern have not, to date, been used in any formal way for interpreting EFM [42]. We believe, this fact explains the inability of EFM to have a high level of sensitivity for detecting the truly at risk fetus. By analogy, the biochemical parameters (free β-hCG and PAPP-A) and nuchal translucency ultrasound were developed independently for Down syndrome screening. When they were finally combined for a single risk score, the performance metrics dramatically improved. We

reach the same conclusion here. Furthermore, using the same analogy, a combined score likelihood ratio of 2.0 would not increase the risk of a 24-year-old into the abnormal range, but it would do so for a 34-year-old. For the FRI, the underlying risk of the fetus is incorporated into the formal risk assessment, and it appears to produce more reliable screening.

These data for the development of a dynamic screening test with a sensitivity for neurological injury and subsequent handicap substantially improved over the system using Categories I–III appear promising. Prospectively, the FRI improves identification of patients at significant risk of fetal intolerance to the hypoxemic and mechanical forces of labor far earlier than Category III. The FRI also avoids the ambiguity of the overly broad Category II whose 80% incidence is much too high to be useful as a screening test. The FRI builds upon the features of the category system on to which additional parameters are added in a new paradigm of fetal surveillance.

The FRI is designed to recognize risk before significant hypoxia or ischemic threat and to prevent the fetus from falling behind by keeping it out of harm's way from the outset. The multicomponent FRI also demonstrates that combining the traditional EFM approach (with MOFR) should provide better statistical performance than EFM alone.

The physiology underpinning this approach is reflected in the consistent progression of the FRI to the point of fetal injury, irrespective of the time in labor or the final heart rate patterns. We believe that the general progression of labor-related fetal injury goes: green, yellow, red (by FRI), then point A, prolonged red stage, point B. Compared to ACOG Category I–III, FRI showed greater sensitivity and specificity. We certainly do not expect a 100% sensitivity of any screening tests to remain, but the improvement over the category system is substantial.

The FRI data suggest that category III and HIE have cutoffs that are far too right on the distribution curve of values. It would be analogous to MSAFP screening for neural tube defects, to using a cut of 4 MOM instead of the typical 2.5 MOM. The sensitivity would be lowered from approximately 90 to 60%. While the PPV of cases above that cutoff would be very high, there would be far too many false negatives and thus a lowered sensitivity. However, unlike MSAFP which has back-up with ultrasound studies and amniotic fluid parameters, as a practical matter, currently used, EFM is effectively treated as a "diagnostic test" and as the last line of defense to prevent potential injury in labor. The FRI methodology suggests that prenatal screening should place more emphasis on identifying the fetus at risk for further decompensation, instead of using it to diagnose definitively the asphyxiated fetus. The FRI seems to allow the clinician increased time to implement fetal therapeutic IR measures (reducing contraction frequency and pushing, improving oxygen and fluid administration, but perhaps most importantly in the 2nd stage, curtailing expulsive efforts, at least temporarily) that may hopefully allow the fetus to accommodate for the greater forces acting upon it and safely deliver vaginally before the threatened fetus becomes asphyxiated or neurologically injured. FRI changes occur long before reaching Category III by which time, it seems to be too late to prevent injury.

EXUA, with its implications for uterine and fetal cerebral blood flow, was assessed according to Table 2b. For the purposes of this report, we have avoided the terms "hyperstimulation" and "tachysystole" as single terms to describe EXUA. The ACOG definition of tachysystole of a frequency of 6+ contractions in 10 min averaged over 30 min appears to us to be too restrictive when compared to the current AWHONN guidelines which call for a maximum of 4 contractions in 10 min, irrespective of FHR pattern. The FRI does not require any changes in the FHR pattern required to make the diagnosis of EXUA, but the data suggest that by reducing the contraction frequency and prolonging the rest time between contractions and/or pushing to meet the criteria of EXUA results in an earlier detection of fetal risk and thereby increases fetal safety as well as the opportunity for successful vaginal delivery when IR measures are implemented in a timely fashion.

Reliance upon the FRI requires a normal admission tracing without suggestion of any preceding insult so that neurologically injured fetuses prior to the onset of labor will not confuse or reduce the successful identification of the fetuses at risk for injury during labor. Patients with abnormal tracings at the outset of labor have significant differences in management and outcomes and therefore were not included in this initial study [43, 44]. In this study, all cases had normal brain structure and function at the outset (reactive nonstress test) and, by clinical, neurological, neuroradiological, and follow-up criteria, were found to have suffered injury during labor and delivery.

We believe this study to be the first one to formally explore the combination of EFM, MOFR, and postnatal neurological factors with known, long-term, radiologically confirmed, neurological handicap without first stratifying the patients according to the severity of metabolic acidemia or encephalopathy at birth. We also believe it is the first study to systematically attempt to use

the EFM parameters as a dynamic "screening" rather than a "diagnostic" test for the diagnosis of injury separate from acidemia. Future, prospective studies will be needed to verify this new use of EFM parameters in conjunction with clinical risk factors.

The NEACP criteria would have only identified (and perhaps demanded intervention in) at most 30%, and category III only 44% of these, whereas our system picked up and would have mandated diligence for all 50 cases as being at very high risk – and did so an average of 6.3 h before delivery and 5.1 h before the appearance of point B. In the 2 patients in whom injury was identified, but point B was not specifically identified, it was the maternal heart rate, not the fetal heart rate pattern that was being unknowingly recorded – a feature detected in our system.

Reaching the red zone and time spent in the red zone were markedly different between study and control patients. Only 22% of controls reached the red zone; they remained there for only about 1 h. Only 17 of 200 (8.5%) controls ever got to point A and none to point B. All 50 CP cases reached the red zone and remained there for an average of 6.3 h. After reaching point B, the average time until delivery was 1.3 h.

Conceptually, the system was designed such that entering the red zone signals the need for the presence at the bed side of senior obstetrical providers who can make decisions and implement them quickly. We have found the easiest way to understand the approach comes through a couple of sports analogies. Thus, the red zone starts a countdown to required action similar to the "shot clock" in basketball. We also believe, using an American football analogy, that getting into the red zone is not 4th down and 15 to go, it is more like 3rd down and 15, i.e. we have to do something now, but immediate cesarean section is not the only option. For the rest of the world, the football analogy is the difference between defending a corner kick rather than a penalty kick.

Conceptually, the argument behind the FRI provides an ongoing dynamic, (not static) multiphasic, easily graphed screening test to assist the clinician in anticipating, early in the course, hypoxic/ischemic, mechanical, and infectious risks to prevent fetal injury [5] rather than tolerating getting close to the edge of some "asphyxial pattern" (Category III) or labor futility before intervention [45]. Clinical management should not be a question of "how much more can the fetus take," but the early identification of the fetus that is on a downward trajectory when potentially hostile mechanical or hypoxic features can be avoided or corrected by timely IR. There would seem to be little justification for waiting until the fetus is indeed acidemic before intervening or before terminal bradycardia supervenes [46, 47].

Strengths of our study include it being one of the largest case series of neurologically injured outcomes in which the fetus entered labor intact, then had non-reassuring EFM changes, and who had pediatric/neurological diagnoses of CP confirmed by both neuroradiology and long-term follow-up. The FRI builds upon existing dogma, and we believe enhances screening capabilities by combining 2 different components of assessment as has been shown to be very useful in genetic screening. Limitations include the retrospective, unique data set, imperfect control group, and sample size big enough to suggest validity of the concept, but not large enough for precise calibration of the individual variables. Currently, all risk factors are weighted evenly. We anticipate that as data accumulate, the exact components and weighting of the FRI may evolve for better statistical modeling and performance.

Our system is intended to replace very subjective and sometimes contradictory approaches of labor management with a more objective one that can be readily graphed to make it easy to follow the course of labor. The FRI parameters are quantifiable with outputs interpretable easily by clinical personnel with varying degrees of training and experience. We have incorporated the FRI parameters into a computerized tracing interpretation program and scoring system. The objective is to improve perinatal outcomes by creating a standardized, quantitative, physiologically based algorithm as a "screening test" that provides time for action before permanent damage occurs.

A few months prior to this publication, Clark's group attempted to optimize EFM performance statistics by using internationally recognized experts to perform the interpretations [15]. These authors have been considered key opinion leaders favoring "traditional" interpretations of EFM including metabolic acidosis as the end point required for labor related HIE (rather than injury per se), and espoused the ACOG category system. However, they reported that even they could only do a little better than standard practice. They concluded: "Of infants born with metabolic acidosis, only approximately one half potentially could be identified and have delivery expedited even under ideal circumstances, which are probably not realistic under current US practice. This represents the limits of EFM performance. Additional technologies will be necessary if the goal of the prevention of neonatal metabolic acidemia is to be realized."

We completely agree with them. We believe, however, that the conceptual framework must shift from EFM as a nuanced, highly subjective Rorschach test into a laboratory-like, multicomponent quantitative algorithm with substantially improved statistical performance to improve public health and prevent at least some of the damage before it occurs rather than identifying it afterwards [48]. This concept is exactly similar to what happened to acute myocardial infarction which in the 1970s went from primarily being a clinical diagnosis into a laboratory one [49].

We believe this paper is a first step towards a re-engineering of the concept of intrapartum surveillance. Further studies will be needed to test and refine these concepts. The stakes are high.

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References

1 Resnik R: Electronic fetal monitoring: the debate goes on... and on... and on. Obstet Gynecol 2013;121:917–918.
2 Sartwelle TP: Electronic fetal monitoring: a defense lawyer's view. Rev Obstet Gynecol 2012;5:e121–e125.
3 Ananth CV, Chauhan SP, Chen HY, D'Alton ME, Vintzileos AM: Electronic fetal monitoring in the United States: temporal trends and adverse perinatal outcomes. Obstet Gynecol 2013;121:927–933.
4 Alfirevic Z, Devane D, Gyte GM: Continuous cardiotocography (CTG) as a form of electronic fetal monitoring (EFM) for fetal assessment during labour. Cochrane Database Syst Rev 2006;3:CD006066.
5 Grimes DA, Peipert JF: Electronic fetal monitoring as a public health screening program: the arithmetic of failure. Obstet Gynecol 2010;116:1397–1400.
6 Ayres de Campos D, Bernardes J, Costa Pereira A, Pereira Leite L: Inconsistencies in classification by experts of cardiotocograms and subsequent clinical decision. Br J Obstet Gynaecol 1999;106:1307–1310.
7 Nelson KB, Dambrosia JM, Ting TY, Grether JK: Uncertain value of electronic fetal monitoring in predicting cerebral palsy. N Engl J Med 1996;334:613–618.
8 Graham EM, Adami RR, McKenney SL, Jennings JM, Burd I, Witter FR: Diagnostic accuracy of fetal heart rate monitoring in the identification of neonatal encephalopathy. Obstet Gynecol 2014;124:507–513.
9 Macones GA, Hankins GD, Spong CY, Hauth J, Moore T: The 2008 National Institute of Child Health and Human Development workshop report on electronic fetal monitoring: update on definitions, interpretation, and research guidelines. J Obstet Gynecol Neonatal Nurs 2008;37:510–515.
10 Clark SL, Nageotte MP, Garite TJ, et al: Intrapartum management of category II fetal heart rate tracings: towards standardization of care. Am J Obstet Gynecol 2013;209:89–97.
11 Parer JT, King T, Flanders S, Fox M, Kilpatrick SJ: Fetal acidemia and electronic fetal heart rate patterns: is there evidence of an association? J Matern Fetal Neonatal Med 2006; 19:289–294.
12 RAZCOG: Intrapartum Fetal Surveillance Clinical Guidelines, ed 3. East Melbourne, The Royal Australian and New Zealand College of Obstetricians and Gynaecologists, 2014.
13 NICE: Intrapartum Care Clinical Guideline National Institute for Health and Care Excellence. London, National Institute for Health and Care Excellence, 2014.
14 Ayres-de-Campos D, Spong CY, Chandraharan E: FIGO consensus guidelines on intrapartum fetal monitoring: cardiotocography. Int J Gynaecol Obstet 2015;131:13–24.
15 Clark SL, Hamilton E, Garite TJ, Timmins A, Warrick PA, Smith S: The limits of electronic fetal heart rate monitoring in the prevention of neonatal metabolic acidemia. Am J Obstet Gynecol 2017;216:163.e1–163.e6.
16 Leigh S, Granby P, Turner M, Wieteska S, Haycox A, Collins B: The incidence and implications of cerebral palsy following potentially avoidable obstetric complications: a preliminary burden of disease study. BJOG 2014; 121:1720–1728.
17 Buttigieg GG: The shifting sands of medicolegal intra-partum Ctg (I-P Ctg) monitoring. Med Leg J 2016;84:42–45.
18 Williams B, Arulkumaran S: Cardiotocography and medicolegal issues. Best Pract Res Clin Obstet Gynaecol 2004;18:457–466.
19 Leveno KJ, Nelson DB, McIntire DD: Second-stage labor: how long is too long? Am J Obstet Gynecol 2016;214:484–489.
20 Spong CY, Berghella V, Wenstrom KD, Mercer BM, Saade GR: Preventing the first cesarean delivery: summary of a joint Eunice Kennedy Shriver National Institute of Child Health and Human Development, Society for Maternal-Fetal Medicine, and American College of Obstetricians and Gynecologists workshop. In reply. Obstet Gynecol 2013;121:687.
21 Bannerman CG, Grobman WA, Antoniewicz L, Hutchinson M, Blackwell S: Assessment of the concordance among 2-tier, 3-tier, and 5-tier fetal heart rate classification systems. Am J Obstet Gynecol 2011;205:288e1–e4.
22 ACOG Practice Bulletin No. 106: Intrapartum fetal heart rate monitoring: nomenclature, interpretation, and general management principles. Obstet Gynecol 2009;114:192–202.
23 ACOG: Neonatal Encephalopathy and Cerebral Palsy: Defining the Pathogenesis and Pathophysiology. Washington, ACOG, 2003.
24 Jenniskens K, Janssen PA: Newborn outcomes in British Columbia after caesarean section for non-reassuring fetal status. J Obstet Gynaecol Can 2015;37:207–213.
25 Jonsson M, Agren J, Norden-Lindeberg S, Ohlin A, Hanson U: Neonatal encephalopathy and the association to asphyxia in labor. Am J Obstet Gynecol 2014;211:667.e1–e8.
26 Marti Gamboa S, Gimenez OR, Mancho JP, Moros ML, Sada JR, Mateo SC: Diagnostic accuracy of the FIGO and the 5-tier fetal heart rate classification systems in the detection of neonatal acidemia. Am J Perinatol 2017;34: 508–514.
27 Phelan JP: Labor admission test. Clin Perinatol 1994;21:879–885.
28 Rochard F, Schifrin BS, Goupil F, Legrand H, Blottiere J, Sureau C: Nonstressed fetal heart rate monitoring in the antepartum period. Am J Obstet Gynecol 1976;126:699–706.

29 Devoe LD: Clinical implications of prospective antepartum fetal heart rate testing. Am J Obstet Gynecol 1980;137:983–990.
30 Korst LM, Phelan JP, Wang YM, Martin GI, Ahn MO: Acute fetal asphyxia and permanent brain injury: a retrospective analysis of current indicators. J Matern Fetal Med 1999;8:101–106.
31 Hobel CJ: Intrapartum clinical assessment of fetal distress. Am J Obstet Gynecol 1971;110:336–342.
32 Tolcher MC, Torbenson VE, Weaver AL, et al: Impact of a labor and delivery safety bundle on a modified adverse outcomes index. Am J Obstet Gynecol 2016;214:401e1–e9.
33 Sarnat HB, Sarnat MS: Neonatal encephalopathy following fetal distress. A clinical and electroencephalographic study. Arch Neurol 1976;33:696–705.
34 Cibils LA: Clinical significance of fetal heart rate patterns during labor. V. Variable decelerations. Am J Obstet Gynecol 1978;132:791–805.
35 Pinas A, Chandraharan E: Continuous cardiotocography during labour: analysis, classification and management. Best Pract Res Clin Obstet Gynaecol 2016;30:33–47.
36 Schifrin BS, Ater S: Fetal hypoxic and ischemic injuries. Curr Opin Obstet Gynecol 2006;18:112–122.
37 Neal JL, Ryan SL, Lowe NK, et al: Labor dystocia: uses of related nomenclature. J Midwifery Womens Health 2015;60:485–498.
38 Cohen WR, Friedman EA: Perils of the new labor management guidelines. Am J Obstet Gynecol 2015;212:420–427.
39 Friedman EA: Disordered labor: objective evaluation and management. J Fam Pract 1975;2:167–172.
40 ACOG: Neonatal Encephalopathy and Neurologic Outcome. Washington, ACOG, 2014.
41 Bakker PC, van Geijn HP: Uterine activity: implications for the condition of the fetus. J Perinat Med 2008;36:30–37.
42 Cahill A, Macones G, McKinstry RC, Smyser CD, Mathur A: EFM and peripartum factors associated with brain injury in term infants. Am J Obstet Gynecol 2015;212:S5.
43 Jonsson M, Agren J, Norden-Lindeberg S, Ohlin A, Hanson U: Neonatal encephalopathy and the association to asphyxia in labor. Am J Obstet Gynecol 2014;211:667.e1–e8.
44 Holmgren CM, Esplin MS, Jackson M, et al: A risk stratification model to predict adverse neonatal outcome in labor. J Perinatol 2013;33:914–918.
45 Bofill JA, Darby MM, Castillo J, Sawardecker SU, Magann EF, Morrison JC: Tachysystole following cervical ripening and induction of labor is not associated with adverse outcomes. Gynecol Obstet Invest, Epub ahead of print.
46 Low JA, Pickersgill H, Killen H, Derrick EJ: The prediction and prevention of intrapartum fetal asphyxia in term pregnancies. Am J Obstet Gynecol 2001;184:724–730.
47 Williams KP, Galerneau F: Fetal heart rate parameters predictive of neonatal outcome in the presence of a prolonged deceleration. Obstet Gynecol 2002;100:951–954.
48 Schifrin BS, Koos B: Defining the limits of electronic fetal heart rate. Am J Obstet Gynecol, in press.
49 Galen RS, Reiffel JA, Gambino R: Diagnosis of acute myocardial infarction. Relative efficacy of serum enzyme and isoenzyme measurements. JAMA 1975;232:147–147.