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Accuracy of Frequency-Related Parameters of the Electrohysterogram for Predicting Preterm Delivery

A Review of the Literature

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The diagnosis of labor and effective prevention of preterm delivery are still among the most significant problems faced by obstetricians. Currently, there is no technique or method for objectively monitoring the uterus and assessing whether the organ has entered a state of increased activity that may indicate labor. Several studies have investigated a new, noninvasive technique to monitor uterine contractions: the electrohysterogram (EHG). Analysis of frequency-related parameters of the EHG may allow physiological uterine activity to be distinguished from uterine contractions that will lead to preterm delivery. However, although a variety of parameters and methodologies have been employed, they have not been objectively compared.

The objective of this review, which was based on a systematic literature search using the Cochrane, PubMed, and EMBASE databases up to February 2008, was to determine whether frequency-related parameters of the EHG signal can reliably differentiate preterm contractions that will lead to preterm delivery from those that will not (in patients who will ultimately deliver at term) and to identify the most accurate parameter.

Of all the different EHG parameters, both human and animal studies indicate that the power spectral density peak frequency may be the most predictive of true labor. The best parameter for predicting delivery is, therefore, related to the EHG spectral content shift, as calculated by Fourier transform, time-frequency, or Wavelet analysis. The incidence and extent to which shifts in uterine electrical spectral components occur, as the measurement-to-delivery interval decreases, imply that these changes might be used to predict preterm delivery. There is also promising data suggesting that a combination of the measured parameters, used as inputs to artificial neural network algorithms, may be more useful than individual ones for critically assessing uterine activity.

Target Audience: Obstetricians & Gynecologists, Family Physicians

Learning Objectives: After completion of this article, the reader will be able to recall the physiology of uterine contractions leading to labor, summarize the limitations of tocodynamometry, and outline four different electrohysterogram parameters.

Preterm birth is a leading cause of neonatal mortality and morbidity (1), and the accurate diagnosis of preterm labor is one of the most significant problems faced by obstetricians. Preterm labor, which occurs in about 10% of pregnant patients, is difficult to predict, assess, and treat (2). Currently, there is no technique for objectively monitoring the uterus and assessing whether the organ has entered a state of increased activity and responsiveness that may require treatment (2). This is particularly important considering that the effectiveness of tocolytic agents depends on early initiation of therapy (1).

The devices and methods currently used for predicting preterm delivery, such as vaginal examination, tocodynamometer, fetal fibronectin, and ultrasound, are somewhat subjective or do not provide accurate diagnosis or prediction of preterm labor (3,27,28). Intrauterine pressure catheters are limited by their invasiveness and the need for ruptured membranes. External uterine monitors, such as tocodynamometers, are uncomfortable, often inaccurate, and depend on a subjective interpretation by the examiner. Biological tests, such as fetal fibronectin, have been used for prognosis, although with unimpressive likelihood ratios (4,27). Linhart et al (4) showed that even cervical change may not be an accurate indicator of true labor, as a large percentage of women with established cervical change do not deliver preterm even if not treated with tocolytics.

When evaluating women with preterm contractions, the clinician's daily dilemma is to differentiate preterm contractions that are simply unproductive physiological uterine activity from effective contractions, capable of inducing progressive cervical dilatation, and leading to delivery. Because current methods cannot discriminate between these 2 types of contractions, most obstetricians either treat all patients having preterm contractions or wait for cervical change. This leads to overtreatment as well as undertreatment. Delay in the diagnosis of preterm labor may result in lower efficacy of tocolytic drugs (5,6), whereas administering tocolysis to all patients exhibiting uterine activity entails risks for mother and fetus (6). Therefore, it is necessary to develop new methods for direct measurement of the uterine properties that distinguish physiological preterm contractions from true preterm labor.

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PHYSIOLOGY OF UTERINE CONTRACTIONS

The mechanical contraction of the uterus is the direct consequence of the propagation of spontaneous electrical activity through the myometrial cells, in the form of intermittent bursts of action potentials (7–9). The force generated by the uterus is related both to the degree to which the action potentials are propagated, which is reflected in the spectral characteristic of the electrohysterogram (EHG) signal, and to the recruitment of additional muscle cells, which influences the signal amplitude (9,10).

It has been demonstrated (11–14) that parturition is a 2-step process consisting of a conditioning (preparatory) phase, followed by active labor. During the conditioning phase, there is a progression of uterine contractility from an inactive to a vigorously active state. In the myometrium, the preparatory process involves changes in transduction mechanisms and the synthesis of several new proteins. As delivery approaches, cell-to-cell gap junctions form and voltage-dependent calcium channels increase, creating the electrical syncytium that is required for effective contractions (14–18). At some point, the conditioning process becomes irreversible and leads to active labor. Uterine electrical activity then becomes more and more synchronous, acting toward complete dilation of the cervix and expulsion of the fetus (19).

ELECTROHYSTEROGRAPHY

Wolfs et al (18) showed that uterine electrical activity could be measured by placing electrodes directly on the uterus. More recently, studies have demonstrated that uterine electrical activity or the EHG, which reflects the sum of the electrical activities of the uterine cells underlying the electrodes, can also be recorded by electrodes placed on the abdominal wall (2,14,20–24). A study by Gondry et al (25) showed that the EHG can be measured as early as 19 weeks of gestation.

Because the EHG signal represents the myometrial bioelectrical activity that triggers the mechanical contraction of the uterus, the parameters of EHG signals recorded during preterm contractions might provide an effective tool for the diagnosis of preterm labor and prediction of preterm delivery.

Several studies have investigated the EHG signal for identifying and predicting labor and discriminating preterm contractions that will lead to preterm delivery from those that will not. Many parameters derived from the EHG signal have been considered, with most related either to timing (21,26,35) or frequency (19,21,26,29–32,34,35,39). Doret et al (19) have clarified that frequency-related parameters are among the earliest observable characteristics as the uterus readies for labor and delivery. Compared to parameters related to the amplitude of the EHG signal, frequency-related parameters are expected to be more comparable from one subject to another and less sensitive to sensor position (20,21,33,36).

SOURCES

The goal of this systematic review was to assess whether frequency-related parameters of the EHG signal can reliably differentiate between preterm contractions that will lead to preterm delivery from those that will not (in pregnancies that ultimately deliver at term) and to identify the most predictive parameters.

We selected all published studies meeting the following inclusion criteria.

Inclusion of women with a gestational age <37 weeks with spontaneous preterm contractions
Transabdominal recording of the uterine EHG activity using contact electrodes
Frequency analysis of the EHG

The outcome measures of interest were occurrence of preterm birth and the corresponding test properties of frequency-related parameters of the EHG. We performed a systematic search in the electronic databases CENTRAL (The Cochrane Library), PubMed, and EMBASE up to February 2008, restricted to the English language. The following keywords were used: frequency analysis, spectral analysis, uterine contraction, preterm contraction, premature obstetric labor, uterine monitoring, electromyography, and electrohysterography (if appropriate, MeSH terms were used). Some references cited in selected and related articles were also searched. Assessment for inclusion and data extraction were performed independently by 2 of the authors. There was no disagreement on the inclusion or data extraction. After inclusion, the quality of the included studies was evaluated.

DESCRIPTION OF THE REVIEWED STUDIES

The technical terms employed in the description are explained and defined in alphabetical order in the Glossary at the end of the manuscript.

General Characteristics

Table 1 lists the characteristics of the studies included in this review, which focuses on frequency analysis of the EHG signal. All studies included pregnant women at 18- to 37-week gestation who were admitted to the hospital with spontaneous preterm uterine contractions. For each study, the uterine electrical activity of at least 2 of the following groups was analyzed and compared: patients in spontaneous preterm labor who delivered preterm, patients not in labor who delivered preterm, patients not in labor who eventually delivered at term, and patients in spontaneous labor at term. All patients provided written informed consent for study participation. Only 2 studies (29,31) mentioned specific inclusion and exclusion criteria. Verdenik et al (31) excluded patients with “severe obstetric pathology,” cervical dilatation over 3 cm, and induced preterm labor. Maner et al (29) excluded patients with “unusual distress” (not defined) and patients weighing more than 105 kg. All studies, except 1 (37), mentioned simultaneous treatment with drugs and other possible confounding factors. All studies evaluated frequency parameters derived from EHG signal analysis, including the frequency of the action potentials within the burst and the frequency of the burst (38). In particular, most of the reviewed studies focused on peak amplitude and peak frequency of the action potentials within the burst. The frequency of the burst was usually expressed as the number of bursts in 10 minutes, which corresponds to the number of contractions in 10 minutes. Most of the studies also included some time-related parameters such as burst duration, the root mean squared value (RMS), or ratios between the calculated parameters (37). All but 1 study (31), which analyzed the uterine electrical activity in total, analyzed uterine EMG activity for each separate burst. In 3 studies, uterine mechanical activity was simultaneously recorded by an external tocodynamometer (31,37,40), and 1 study recorded the patient’s perception of contractions (41).

Bipolar electrodes were used in all studies, with an inter-electrode distance ranging from 2.5 to 7 cm. The duration of measurement varied from 20 to 120 minutes. Band-pass filtering and sampling frequency of the EHG signal were different in all studies, varying in the range of 0.05 to 16 Hz and 16 to 32 Hz, respectively.

Analysis of the EHG

Buhimschi et al (40) computed the Fast Fourier transform of the single EHG signal burst. For each

TABLE 1
Characteristics of included studies

	Study Population				Recording Method (Electrode Type, Electrode Distance, Duration)	Comparison	Analyzing Method (Analyzed Frequency Band (B), Sampling, Frequency (Fs))	Outcome Parameter of the EHG Signal
	No. Patients	Reason of Admission, Gestational Age, Treatment	Inclusion Criteria	Exclusion Criteria				
Buhimschi 1997	40 (total) ● 23 active term ● 5 preterm ● 1 failed induced labor ● 3 postpartum ● 5 longitudinal ● 3 at GA 24 weeks	● Spontaneous uterine contractions ● GA 20–43 week ● Oxytocin (n = 4), EDA (n = 4): unclear in what patients	● Unclear	● Severe obstetric pathology ● Unusual patient distress	● 4 bipolar electrodes ● 5 cm apart ● 20–120 min	● CTG (n = 17) ● IUP (n = 5) ● Unclear in which patients	● FFT ● B = 0.3–50 Hz	● PDS peak amplitude ● PDS peak frequency ● Burst frequency
Leman 1998	42 (total) ● 29 term ● 12 preterm ● 1 abortion	● Preterm contractions ● GA 21–37 week ● 48 h betamimetic	● Unclear	● Twin pregnancy ● Medical abortion	● 2 bipolar electrodes ● 2.5 cm apart ● 60–120 min	● Patient's perception	● Wavelet transform ● B = 0.2–8 Hz ● F_s = 16	● Contraction duration ● Relative magnitude of contraction ● Energy of the signal in different frequency bands (0–3 Hz) ● Minimum+maximum Instantaneous Frequencies and associated time
Verdenik 2001	47 (total) ● 30 term ● 17 preterm	● Preterm contractions ● GA 25–35 week ● After measurement (tocolytics, 17%; spasmolytics, 49%; dexamethasone,15%)	● Contractions confirmed by TOCO ● Hospitalization on obstetrician's view	● Severe obstetric pathology ● Cervical dilatation over 3 cm ● Induced preterm labor	● Bipolar electrodes ● 7 cm apart ● 30 min	● CTG	● Logistic regression ● Median frequency ● B = 0.1–4 Hz ● F_s = 20 Hz	● Root mean square value ● Median frequency
Maner 2003	99 (total) ● 57 term ● 42 preterm	● Preterm contractions ● GA 24–37 week ● Unclear	● Singleton gestation ● Ultimate spontaneous vaginal delivery ● Intact membranes ● Cervical dilatation <2 ● Effacement <80% ● No signs of infection	● Unusual patient distress ● Patients weight >105 kg	● 4 bipolar electrodes ● 3 cm apart ● 30 min	● CTG	● FFT ● B = 0.34–1.0 Hz ● F_s = 100 Hz	● PDS peak frequency ● PDS peak amplitude
Marque 2007	107 (total) ● 71 term ● 36 preterm	● Preterm contractions ● GA 18–37 wk ● Unclear	● Unclear	● Unclear	● Bipolar electrodes ● Duration unclear ● 2.5 cm apart	● Unclear	● Wavelet transform ● Artificial neural network ● B = 0.05–16 Hz ● F_s = 32 Hz	Energy of the signal in the low and high frequency band
Maner 2007	185 (total) ● 134 term ● 51 preterm	● Preterm contractions ● Only patients with clear clinical determination ● Unclear	● Patients for whom a clear clinical determination of labor or non-labor could be made	● Unclear	● 4 bipolar electrodes ● 6.35 cm apart ● At least 30 min	● CTG ● Manual ● Determination by investigators	● FFT ● Artificial neural networks ● B = 0.34–1.0 Hz ● F_s = 100 Hz	● PDS peak frequency ● Standard deviation of burst duration ● Ratio PDS peak frequency/standard deviation burst duration ● Burst frequency ● Burst duration ● Total activity

individual patient, at least 3 bursts were analyzed in order to extract the peak amplitude of the power density spectrum (PDS) and the average peak frequency (fP). The frequency of the bursts per 10 minutes and the duration of each burst were also considered. Four groups of patients were studied: preterm laboring, preterm nonlaboring, term laboring, and term nonlaboring. The values of the parameters obtained from the patients in each group were averaged and their standard deviations calculated. When values from the 4 groups were compared, the duration of the bursts was similar before and during labor in both term and preterm patients. However, the frequency of the bursts per 10 minutes was significantly higher in laboring patients who delivered, either at term (3.75 ± 0.27) or preterm (3.70 ± 0.30), than in nonlaboring patients who delivered at term (0.89 ± 0.44) or preterm (0.50 ± 0.17). In nonlaboring preterm patients, the peak amplitude of the PDS (11.36 ± 4.03 μV) was reached at a frequency fP = 0.42 ± 0.02 Hz, whereas nonlaboring patients at term exhibited a significantly higher peak amplitude (14.11 ± 2.31 μV) at a higher frequency (fP = 0.48 ± 0.003 Hz). During labor, the peak amplitude increased significantly and similarly for both term (60.20 ± 13.87 μV) and preterm (62.27 ± 22.93 μV) subjects, at correspondingly higher peak frequencies (fP = 0.71 ± 0.005 Hz and fP = 0.78 ± 0.006 Hz, respectively).

These results are in agreement with the work of Maner et al (29) who studied only nonlaboring patients with intact membranes and cervical dilatation of 2 cm or less. The peak frequency of the EHG signal was calculated for both the term and preterm groups, using a method similar to that used by Buhimschi et al (40), and term patients were divided into 2 subgroups: ≤24 hours from recording to spontaneous delivery, and >24 hours from recording to spontaneous delivery. These investigators showed that the peak frequency within the EHG bursts (fP) increased as the measurement-to-delivery interval decreased. The fP was higher in patients within 24 hours of delivery (fP = 0.4768 ± 0.0144 Hz), than in those who were ≥24 hours of delivery (fP = 0.4042 ± 0.0185 Hz).

Preterm subjects were also divided into 2 subgroups: ≤4 days to spontaneous delivery and >4 days to spontaneous delivery. Similar to the patients at term, the fP was higher in patients within 4 days of delivery (fP = 0.5113 ± 0.0279 Hz) than in those who were >4 days from delivery (fP = 0.3899 ± 0.0061 Hz). The fP in preterm patients who were ≤24 hours from delivery was similar to the peak frequency in term patients who were ≤24 hours from delivery.

The parameters measured in the preterm patients who were ≤4 days from spontaneous delivery had 60.0% sensitivity and 96.9% specificity for predicting delivery; positive and negative predictive values were 85.7% and 88.6%, respectively (Table 2). Positive and negative likelihood ratios were calculated to be 19.35 and 0.41, respectively.

The parameters measured in the term patients who were ≤24 hours from spontaneous delivery had 97.6% sensitivity and 53.3% specificity for predicting delivery, with positive and negative predictive values of 85.4% and 88.9%, respectively. Positive and negative likelihood ratios were calculated to be 2.09 and 0.05 respectively.

In a more recent study (37), Maner et al used artificial neural network algorithms to show that peak frequency (fP), the standard deviation of the burst duration, and the ratio of these 2 parameters are the best uterine EHG parameters for classifying patients as laboring or nonlaboring. The subjects enrolled in the study were divided into 4 groups: preterm nonlaboring, preterm laboring, term nonlaboring, and term laboring. The fP was significantly higher for laboring patients both at term (fP = 0.4371 ± 0.0449 Hz) and preterm (fP = 0.4708 ± 0.0459 Hz), com-

TABLE 2
Predictive measures of EHG parameters

	Sensitivity (Se)	Specificity (Sp)	Positive Predictive Value (PPV)	Negative Predictive Value (NPV)	LR+	LR−
Buhimschi 1997	Nc	Nc	Nc	Nc	Nc	Nc
Leman 1998	Nc	Nc	Nc	Nc	Nc	Nc
Verdenik 2001	47.1%	90.0%	72.2%	75%	4.71*	0.59*
Maner 2003	60.0%	96.9%	85.7%	88.6%	19.35*	0.41*
Marque 2007	90%†	91%	Nc	92%	10*	0.11*
Maner 2007	92.3%	71.1%	52.2%*	96.4%*	3.19*	0.11*

*Calculation by reviewers.
†Best results.
Nc indicates not calculated.

pared with patients who were nonlaboring at term (fP = 0.3916 ± 0.0223 Hz) and nonlaboring preterm (fP = 0.3982 ± 0.0231 Hz). Conversely, the average standard deviation of the burst duration was significantly lower for laboring patients compared with nonlaboring patients in both the preterm and term subgroups. Consequently, the ratios between the fP and the average standard deviation of the burst duration were much higher in the laboring groups compared to the nonlaboring ones. These parameters had 92.3% sensitivity and 71.1% specificity for predicting labor. Positive and negative predictive values were calculated to be 52.2% and 96.4%, and positive and negative likelihood ratios were 3.19 and 0.11, respectively (Table 2).

Verdenik et al (31) evaluated the RMS and the median frequency of the EHG in patients with spontaneous preterm contractions who delivered preterm compared to patients with preterm contractions who did not deliver preterm. A predictive logistic regression model showed that the most important parameter predicting preterm delivery was a high RMS value, which was higher in patients with preterm contractions who delivered preterm than in those who ultimately delivered at term (17.5 ± 7.78 mV vs. 12.2 ± 6.25 mV). The median frequency was similar in the term and preterm groups (0.37 ± 0.049 Hz vs. 0.36 ± 0.068 Hz, respectively). This group also investigated the relationship between the EHG signal parameters and gestational age, and found that the median frequency correlated negatively with the gestational age ($r = -0.234$, $P = 0.113$). The authors concluded that with increasing duration of pregnancy, the frequency content of electrical activity becomes lower, as expressed by a lower median frequency of uterine electrical activity. The RMS value had only a weak, nonsignificant correlation with gestational age ($r = 1.139$; $P = 0.353$). From these results, the authors concluded that during pregnancy, the median frequency decreases continuously and linearly with increasing gestational age, whereas the RMS value increases, but only a few days before the true labor begins. In this study, from a logistic model in which the RMS value was the independent variable, the authors obtained sensitivity and specificity values of 47.1% and 90.0%, respectively, for the prediction of delivery. Positive and negative predictive values were 72.7% and 75.0%, respectively (Table 2), and positive and negative likelihood ratios were calculated to be 4.71 and 0.59, respectively.

Leman et al (41) evaluated a large data set that included time and frequency parameters of the EHG signal in 42 women admitted to the hospital for preterm contractions. The authors performed a discriminant analysis to assess the ability of the selected parameters to predict the evolution of the contractions during pregnancy, and to distinguish patients with preterm contractions who delivered preterm from those who ultimately delivered at term. Among the considered parameters, the authors evaluated the duration of bursts and the energy of the EHG signal recorded in the 2 populations at the same gestational age in each of the frequency bands (0.3–0.6 Hz), (0.6–0.9 Hz), (0.9–1.2 Hz), (1.2–1.5 Hz), and (1.5–3 Hz). When comparing the 2 populations, the contractions recorded in patients with spontaneous preterm contractions who delivered preterm had higher frequencies than those with preterm contractions who delivered at term, that is, had more energy in the 2 higher frequency bands between 1.2 and 3 Hz. When the 2 populations were compared at the same number of weeks before delivery, the investigators found that, as much as 15 weeks before delivery, it was possible to distinguish contractions that lead to preterm delivery from those that did not. However, the difference was observed in different frequency bands; up to 8.5 weeks before delivery, the energy of the EHG signal was generally higher in the preterm contractions/preterm delivery group than in the preterm contractions/term delivery group, in the frequency bands 0.3 to 0.6 Hz and 0.6 to 0.9 Hz.

At 9.5 to 15 weeks before delivery, the duration of the contractions in the preterm contractions/preterm delivery group was shorter than in the preterm contractions/term delivery group. At 2.5 to 4 weeks before delivery, the trend observed in earlier weeks was reversed: the duration of the contractions was longer and the magnitude was higher in the preterm contractions/preterm delivery group, but the energy in the frequency bands 0.3 to 0.6 Hz and 0.6 to 0.9 Hz was generally higher in the preterm contractions/term delivery group than in the preterm contractions/preterm delivery group. At 0.5 to 1 week before delivery, the contractions of preterm and term delivering patients were similar and no discriminant parameters could be found.

The results of Leman's study (41) are in agreement with those of Marque et al (38). Marque et al (38) found that it is possible to detect increased risk of preterm birth by using EHG processing as early as 27 weeks of gestation. From the energy of the signal as calculated by the Wavelet transform in the frequency band between 0.1 and 0.6 Hz and the band between 0.6 and 3 Hz, the authors computed parameters representative of the following: (1) high-risk preterm contractions leading to preterm delivery, and (2) normal or low-risk preterm contractions leading to term delivery. In this study, different neural network algorithms using frequency-related parameters of the EHG for predicting preterm birth were compared. Depending on the algorithm employed, the parameters had 85.0% to 90.0% sensitivity and 91.0%–93.0% specificity for predicting preterm delivery. The negative predictive values were 88.0% to 92.0% (Table 2). The positive and negative likelihood ratios were 10 and 0.11, respectively.

EHG PARAMETERS

PDS Peak Frequency

The most investigated parameter in the literature is the PDS peak frequency. Shifting of the EHG signal energy to a higher frequency as delivery approaches has been observed in both animals and humans. The extent of the peak frequency shift was consistent among all reviewed studies (Table 3). This shift can be explained by the underlying physiology. The frequency of action potentials within a burst is a direct measure of the rate of the depolarization/repolarization process in the myometrial cells, a process largely governed by calcium ion influx across ion channels (42). When modifications in the myometrial cell's plasma membrane ion channel initiate labor, the uterus becomes more excitable (42,43), the signal propagation distance and contraction strength increase, and, as a result, higher frequency cycles within bursts of activity are expected (29,37).

In animal studies (21), it has been shown that the shift to higher frequencies during both term and preterm labor is similar for both uterine and abdominal surface recordings. Buhimschi et al (21) found that most changes in the uterine EHG activity appear in the last 24 hours before delivery. Doret et al (19) identified, in rats, a shift from low (approximately 0.75 Hz) to high (approximately 2.5 Hz) PDS peak frequency 12 hours before delivery and before modifications in other parameters (such as intrauterine pressure integral activity, EMG mean, and EMG PDS energy) could be observed.

TABLE 3
Comparison of values for peak frequency

Study	PDS Peak Frequency (Hz)	
	Preterm Non-Labor	Preterm Labor
Buhimschi 1997	0.42 ± 0.02*	0.78 ± 0.06†
Leman 1999	Nc	Nc
Verdenik 2001	Nc	Nc
Maner 2003	0.3899 ± 0.0061‡	0.5113 ± 0.0279§
Marque 2007	Nc	Nc
Maner 2007	0.3982 ± 0.0231	0.4708 ± 0.0459

*GA 27–36 weeks, n = 5.
†GA 33–36 weeks, n = 4.
‡>4 days before delivery, n = 31.
§<4 days before delivery, n = 11.
Nc indicates not calculated.

The general increase in the PDS peak frequency, observed as the patient enters the final phase of uterine readiness, indicates that a greater fraction of the power of uterine activity resides at higher frequencies in patients just before labor than in those further removed from delivery. This was confirmed by the study of Leman et al (41), who showed that PDS energy increases within 3½ to 7 days before delivery. Garfield et al (30) analyzed EMG bursts and showed that burst energy increases significantly within 48 hours before delivery; at about 1 day before delivery, a shift to high-frequency bursts occurs as the transition to preparedness for labor is made. Maner et al (29) also showed that PDS peak frequency increases as the measurement-to-delivery interval decreases, and identified the best values predicting delivery within 4 days.

Median Frequency

Among the reviewed studies, only Verdenik et al (31) studied the median frequency rather than the peak frequency, and did not analyze each signal burst separately. Perhaps for this reason, these investigators reported a different trend in the frequency content of the EHG signals as a function of the gestational age. In particular, the authors reported that as the pregnancy approaches term, the frequency content of the electrical activity becomes lower.

Frequency of Electrical Bursts

Another frequency-related parameter analyzed in all studies is the frequency of electrical bursts, which is the electrical equivalent of the frequency of contractions measured by a tocodynamometer or by an intrauterine pressure catheter. Unfortunately, the prognostic value of this parameter, which is in principle related to the prognostic value of tocodynamometry, is poor (21,26). It is noteworthy that in all reviewed studies an increase in this parameter occurs as delivery approaches. However, this can be explained by the ever increasing level of uterine contraction coordination that is required for labor and delivery.

PDS Peak Amplitude and RMS Value

The PDS peak amplitude and the RMS value are equivalent representations of the EHG signal energy. The increased energy of the electrical activity results from the changes in the electrical properties of the myometrium that occur during labor and increased current flow in the myometrial muscle. Verdenik et al (31) found that the RMS value is the most important EHG parameter for predicting delivery, whereas Buhimschi et al (40) determined that an increase in the PDS peak amplitude occurs as gestational age increases and delivery approaches. In an earlier study (2), Buhimschi et al demonstrated that an increase in the amplitude of action potentials occurs during the labor that precedes delivery. According to these authors, the action potential amplitude is related to the amplitude of the depolarizing current and establishes the probable distance that an action potential can travel; thus, the higher the amplitude, the greater the action potential distance, which excites remote tissues to produce a more forceful contraction (44). From this, they concluded that conduction velocity is improved during labor. Similar results were reported by Lammers et al (46).

Burst Duration

Burst duration is another parameter that discriminates between preterm contractions that lead to preterm term delivery and those that do not, at 2.5 to 4 weeks before delivery (41). Maner et al (37) used the standard deviation of the burst duration in combination with neural networks, with good results in terms of sensitivity and negative predictive value. In particular, the authors observed that the standard deviation of the burst duration decreases with the progression of pregnancy, or expressed differently, the duration of a contraction is more stable late in pregnancy and during labor. The results of this study are in agreement with observed physiology, as contractions should be more coordinated and synchronous during the labor that precedes delivery. However, contractions are more difficult to detect early in gestation than later in pregnancy or during labor, which may hamper the accuracy of burst duration detection, and thus affect their interpretation. Alternatively, the greater variability of burst duration found earlier in gestation might be related to inaccurate assessment of the duration itself, because of the low energy of the signal.

EVOLUTION OF CONTRACTIONS TOWARD ACTIVE LABOR

The spectral changes in the EHG signal that occur with increasing gestational age have been identified in patients delivering both at term and preterm. Thus, a key issue is to determine whether preterm contractions leading to preterm delivery might simply result from the same process that leads to a delivery at term, but occurring earlier. Maner et al (29) found that there is no significant difference between the average PDS peak frequency in preterm and term patients who are within 24 hours of delivery, and concluded that the 2 groups share a common uterine mechanism, partially independent of gestational age.

This is contrary to the results of Leman et al (41), who found that it is possible to distinguish preterm contractions leading to preterm delivery from preterm contractions that ultimately result in delivery at term, as far in advance as 15 weeks before delivery. However, at about 1 week before true labor begins, the difference in frequency parameters between patients who deliver preterm and those who deliver at term disappears. This is consistent with the hypothesis that the evolution of the 2 pregnancies is different until 1 week from delivery. Then, the 2 groups reach the same stage in preparedness for labor and cannot be distinguished.

CONCLUSION

This review indicates that parameters derived by EHG signal analysis might become an important tool for monitoring uterine contractions, and have the potential to predict delivery (Table 4). In the future, measurement and analysis of EHG signals may be of value to both obstetricians and patients because it allows noninvasive monitoring of uterine electrical activity, the primary source of contractions.

In this overview of all studies using frequency analysis of noninvasively recorded uterine EHG activity in patients at risk for preterm delivery, the clinical value of different EHG parameters was assessed. Of all the different EHG parameters, the studies of Buhimschi et al (40) and Maner et al (29,37) as well as animal studies indicate that PDS peak frequency may be the most predictive of true labor. Laboring preterm patients have a significantly higher PDS peak frequency than nonlaboring patients and, as the measurement-to-delivery interval decreases, a significant shift from low to high PDS peak frequency occurs. As early as 15 weeks before delivery, contractions that will lead to delivery can

TABLE 4
Overview of changes in EHG parameters while comparing active labor with the nonlaboring phase

EHG Parameter	Most Observed Change While Approaching Laboring Phase	Study in Which Parameter is Evaluated	Term Contractions	Preterm Contractions
Burst duration	Increase	Buhimschi		
	Increase at 0.5–1 week before delivery	Leman		
	Decrease in standard deviation with progression of pregnancy	Maner		
Frequency of bursts per 10 min	Increase	Buhimschi	Increase (3.75 ± 0.27 vs. 0.89 ± 0.44 Hz)	Increase (3.70 ± 0.30 vs. 0.50 ± 0.17 Hz)
PDS peak amplitude	Increase	Buhimschi	Increase (60.20 ± 13.87 vs. 14.11 ± 2.31 μV)	Increase (62.27 ± 22.93 vs. 11.36 ± 4.03 μV)
	Increase at 0.5–1 weeks before delivery	Leman		Higher energy in frequency bands 0.3–0.6 Hz and 0.6–0.9 Hz
PDS peak frequency	Increase ≤24 h before delivery	Buhimschi	Increase (0.71 ± 0.005 vs. 0.48 ± 0.003 Hz)	Increase (0.78 ± 0.006 vs. 0.42 ± 0.02 Hz)
	Increase in term patients ≤24 h before delivery	Maner	Increase (0.4768 ± 0.0144 vs. 0.4042 ± 0.0185 Hz)	Increase (0.5113 ± 0.0279 vs. 0.3899 ± 0.0061 Hz)
	Increase in preterm patients ≤4 days before delivery			
	Increase	Maner (37)	Increase (0.4371 ± 0.0449 vs. 0.3916 ± 0.0223 Hz)	Increase (0.4708 ± 0.0459 vs. 0.3982 ± 0.0231 Hz)
RMS value	Increase a few days before delivery	Verdenik		Increase (17.5 ± 7.78 mV vs. 12.2 ± 6.25 mV)
Median frequency	Linearly decrease with increasing gestational age	Verdenik		

be distinguished from those that will not. In addition, a significantly higher spectral energy is found in the 0.3 to 0.6 Hz and 0.6 to 0.9 Hz frequency bands in patients with preterm contractions that will lead to preterm delivery.

Verdenik et al (31) reported that the RMS value was higher in the preterm delivery group than in the term delivery group. Buhimschi et al (40) showed that the PDS peak amplitude rises as gestational age increases and the time to delivery decreases. Burst duration and the frequency of contractions were evaluated in all studies and were shown to increase as the time to delivery approaches. From the studies of Maner et al (37) and Marque et al (38) it could be concluded that the use of artificial neural network may be a powerful method to classifying preterm contractions.

The best parameter for predicting delivery is, therefore, related to the EHG spectral content shift, as calculated by Fourier transform, time-frequency, or Wavelet analysis. The incidence and extent to which shifts in uterine electrical spectral components occur as the measurement-to-delivery interval decreases imply that these changes might be used to predict preterm delivery.

A peak frequency cutoff value that indicates the likelihood of delivery could be an important tool for identifying women with preterm contractions who will undergo transition into the active phase of labor. Unfortunately, based on the studies that were reviewed, this type of universal peak frequency cutoff value has not been identified; a study to determine the optimal cutoff value is greatly needed.

On the other hand, there is promising data suggesting that a combination of the measured parameters, used, for example, as inputs to artificial neural network algorithms, may be more useful than the individual ones for critically assessing uterine activity. Moreover, it is possible that including additional parameters that are representative of the uterine functionality, such as propagation velocity, (2) may result in a fundamental improvement in monitoring patients with preterm contractions. The potential clinical value would be the ability to use objective rather than subjective measurements of uterine electrical activity to evaluate uterine preparedness for labor and the likelihood of delivery.

Glossary

Artificial Neural Network. A mathematical or computational model based on biological neural networks, which in this case can be used to classify uterine activity based on a set of representative parameters put into the neural network. Neural networks learn by example. That is, before using the network for classification, the user transfers representative data and training algorithms to the network, and the network will then automatically learn the structure of the data and use it to correctly classify events.

For example, to distinguish preterm contractions from normal physiological contractions on the basis of parameters derived by the EHG, while training the neural network will be asked to correctly classify preterm or at-term contractions when fed with the parameters derived from those contractions. When operative, a number of chosen parameters derived by an EHG recorded during preterm contractions can be sent to the neural network, and it will classify the outcome as preterm or term delivery based on what it learned during the training algorithm.

Average Peak Frequency. The average value of the frequency, showing the peak energy (peak frequency) estimated from a group of patients or contraction segments.

Burst of Action Potentials. Electrical activity of the uterus, as recorded by the EHG, during the active period of contractions (20). Usually, each electrical burst corresponds to 1 mechanical contraction of the uterus, as detected by a tocodynamometer or by an internal uterine pressure catheter (Fig. 1).

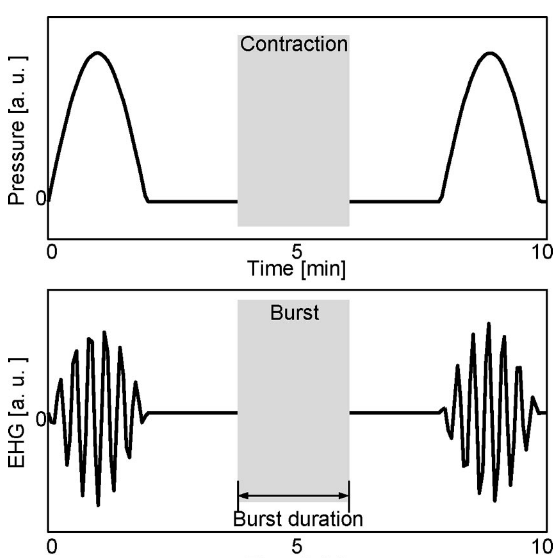

Fig. 1. Schematic representation of contraction as recorded by tocodynamometer (upper trace) and corresponding EHG signal (lower graph).

Burst Duration. The time duration of 1 burst of action potentials (Fig. 1) (20).

Energy. This parameter can be calculated as a function of time, by squaring and integrating the amplitude of the signal in the time domain, or as a function of frequency. For finite energy signals, the energy in the frequency domain can be calculated by squaring and integrating the absolute value of the Fourier transform (48). The time-frequency or the time-scale representation can be used to calculate the signal energy as a function of both frequency and time.

For signals with infinite energy, the concept of power (energy divided by the length of considered signal segment) is introduced (48).

Fourier Transform. A mathematical tool used to analyze the frequency content of a signal. The Fourier transform allows transformation of a function of time into a function of frequency by decomposing the original signal into periodic basis functions, that is, sine and cosine waves. The fast Fourier transform is an efficient algorithm to compute the Fourier transform of discrete signals (48). Calculation of the Fourier transform can be performed to analyze the energy, the power spectral density (PSD), or the peak frequency of the EHG.

Frequency. The frequency of a periodic phenomenon is the number of times the phenomenon occurs within a specified time interval. Signals, however, are not generally characterized by a single frequency, as a sine or a cosine wave, but by a range of frequencies, the frequency band, or by a dominant frequency, that is, a frequency at which the signal energy or the signal amplitude is higher than other frequencies (48).

For example, most of the frequency content of the EHG signal is concentrated in the frequency band between 0 and 3 Hz (41). That is, when computed in the frequency domain, the EHG signal energy will be much higher between 0 and 3 Hz than in other frequency ranges. Furthermore, even within the frequency range between 0 and 3 Hz, each frequency provides a different contribution to the signal, which is proportional to the signal amplitude at that frequency.

Frequency Band. The interval of frequencies between 2 frequency values. The width of the frequency band is called bandwidth.

Some of the reviewed studies (ie, Leman (41) and Marque et al (38)) analyzed the signal energy in specific bands as discriminant EHG parameters for predicting preterm labor. One of the conclusions of Leman's study was that the contractions leading to preterm labor had high frequencies. By comparing the energy of an EHG signal in lower bands between 0.1 and 1.2 Hz and higher bands between 0.6 and 3 Hz, these investigators showed that the signal had more energy in the higher bands when it was derived from preterm contractions that ultimately resulted in preterm delivery. In fact, it has been suggested that the frequency content of the EHG signal can be considered a measure of the level of propagation of action potentials. A signal with higher frequency content suggests that action potentials are propagating effectively in the uterus, producing a coordinated and forceful contraction.

Frequency Analysis or Spectral Analysis. Analysis of the frequency of a signal. It can be performed by Fourier transform to detect the frequency or frequency band at which the energy of a signal is concentrated. This analysis, which is similar to time-scale and time frequency analysis, performed at different gestational ages on preterm/term delivery population, could result in the identification of a peak frequency, or mean frequency, or frequency bands, which are specific of a particular stage of the labor process and could, therefore, be used for the prognosis of labor.

Frequency of Bursts. Number of electric bursts or number of mechanical contractions per time unit (usually per 10 minutes) (20). This parameter is obtained by counting the number of times the uterus contracts and, within a given time period, it corresponds to the parameter that is detected clinically using external tocography.

Frequency Within Bursts. This is the frequency content of the action potentials within the burst, extracted from time segments of the electrical signal (which can include a single or multiple bursts) by frequency analysis, using frequency, time-frequency, or time-scale representations (20). The frequency within the burst is usually measured in Hertz. The parameters that are representative of the frequency content of the action potentials within the burst are the mean, the median, and the peak frequency.

Mean Frequency. Mean value of the signal frequency distribution, that is, distribution of the signal amplitude at different frequencies. For nonstationary signals, such as the EHG, the value of mean frequency varies with time; it can therefore be obtained by time-frequency analysis (45).

Median Frequency. A function of time that represents the frequency below which 50% of the signal PSD is contained. It is obtained by determining the median value of the time-frequency representation (45).

Mother Wavelet. A fast-decaying oscillating waveform (wavelet) of finite length. It can be used in the wavelet transform as prototype function, to decompose a time signal into scaled and translated versions (47).

Peak Frequency. In general, the frequency at which a function of frequency reaches its maximum. In this article, the peak frequency is the frequency at which the PSD reaches its maximum, or the frequency at which the power of the signal is maximum, and therefore the dominant frequency of the signal.

In this review, we note that a shift occurs in the peak frequency from lower to higher frequencies as delivery approaches. The fact that the frequency of the EHG signal increases as delivery approaches can be intuitively explained by more frequent cell-to-cell propagation of action potentials at the myometrial level.

Peak Amplitude. In general, the maximum amplitude of a signal. In this review, we refer to the PSD peak amplitude, which is the maximum value of the PSD.

This parameter, which indicates the maximum power of the signal, has been tested as a way to discriminate between preterm and term contractions. As delivery approaches, it is expected that the EHG peak amplitude will increase as a result of increased myometrial activity. However, because the PSD is an amplitude-related parameter, it can be highly subject dependent.

Power Spectral Density. The power of the signal as a function of frequency. The value of the PSD at each frequency is proportional to the contribution of that frequency to the total power of the signal.

For finite length time-signals, the PSD can be obtained by squaring the absolute value of the Fourier transform, calculated on a signal segment, and dividing it by the length of the considered segment.

RMS Value. The RMS value of a signal is a statistical measure of its amplitude. The RMS value is the square root of the mean of the signal squared. As delivery approaches, the EHG signal amplitude is expected to increase as a result of increased myometrial activity. However, as it is an amplitude-related parameter, it can be highly subject dependent.

Time-Frequency Representation. This parameter quantifies the contribution of each frequency to the energy of the signal at a given time interval. The time-frequency representation of a signal is achieved by the Fourier transform of short time-segments of the original signal, and is therefore a compromise between the frequency and the time resolution of the transformed signal. The time-frequency representation is usually preferred to the Fourier transform when non-stationary signals (eg, EHG) are analyzed (45).

Time-Frequency Analysis. Analysis of a time-frequency representation (45).

Time Resolution Versus Frequency Resolution. Ability to distinguish the signal characteristics at 2 different points in the time or in the frequency domain (45).

The amplitude of the continuous Fourier transform of an infinitely long signal may be considered to be a representation with perfect frequency resolution, but with no time information. The Fourier transform, in fact, conveys information about the average frequency content, but it fails to convey when, in time, different frequencies are present in the signal. Time-frequency analysis and Wavelet analysis provide a bridge between time and frequency representations, because they convey simultaneously some temporal information and some frequency or frequency-related information.

Wavelet Transform (or Wavelet or Time-Scale Representation). This representation of a signal is obtained by decomposing the signal into a sum of the scaled and translated versions (wavelet) of a prototype function called mother wavelet. Conceptually very close to time-frequency distributions, the Wavelet transform can localize the frequency-related properties of the signal in time as it provides a time-scale representation of the signal that can be transformed into a time-frequency representation (47). The Wavelet transform can be used to analyze the energy of a signal as a function of time and frequency.

For example, in the study by Marque et al (38), the Wavelet transform is used to calculate and compare the signal energy in the frequency bands between 0.1 to 0.6 Hz and 0.6 to 3 Hz.

Wavelet Analysis or Time-Scale Analysis. Analysis by the Wavelet transform (or of the time-scale representation).

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