Early Human Development 90 (2014) 81–85

Contents lists available at ScienceDirect

Early Human Development

journal homepage: www.elsevier.com/locate/earlhumdev

Quantitative comparison of entropy analysis of fetal heart rate variability related to the different stages of labor

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ARTICLE INFO

Article history:
Received 31 December 2012
Received in revised form 13 November 2013
Accepted 16 December 2013

Keywords:
Approximate entropy
Sample entropy
Labor progression
Fetal heart rate
Cardiotocography

ABSTRACT

Background: The interpretation of the fetal heart rate (FHR) signal considering labor progression may improve perinatal morbidity and mortality. However, there have been few studies that evaluate the fetus in each labor stage quantitatively.
Aim: To evaluate whether the entropy indices of FHR are different according to labor progression.
Study design: A retrospective comparative study of FHR recordings in three groups: 280 recordings in the second stage of labor before vaginal delivery, 31 recordings in the first stage of labor before emergency cesarean delivery, and 23 recordings in the pre-labor before elective cesarean delivery.
Subjects: The stored FHR recordings of external cardiotocography during labor.
Outcome measures: Approximate entropy (ApEn) and sample entropy (SampEn) for the final 2000 RR intervals.
Results: The median ApEn and SampEn for the 2000 RR intervals showed the lowest values in the second stage of labor, followed by the emergency cesarean group and the elective cesarean group for all time segments (all $P < 0.001$). Also, in the second stage of labor, the final 5 min of 2000 RR intervals had a significantly lower median ApEn (0.49 vs. 0.44, $P = 0.001$) and lower median SampEn (0.34 vs. 0.29, $P < 0.001$) than the initial 5 min of 2000 RR intervals.
Conclusions: Entropy indices of FHR were significantly different according to labor progression. This result supports the necessity of considering labor progression when developing intrapartum fetal monitoring using the entropy indices of FHR.

1. Introduction

Fetal heart rate (FHR) analysis is one of the important methods for evaluating the fetal condition. However, despite the widespread use of electronic FHR monitoring, its effect in decreasing fetal mortality and morbidity has not been established [1]. To reduce inter- and intra-observer variability of visual analysis, computerized analysis was developed, but it did not result in significant clinical improvement [2]. Accordingly, there have been many efforts to develop new monitoring methods more responsive in differentiating between normal and pathological fetal conditions.

Entropy analysis that measures the correction and persistence of a signal is a nonlinear mathematical approach to quantify the irregularity and complexity of a system [3]. Entropy analysis of heart rate is based on a systematical biological theory that suggests weak connections between systems or within a system that are associated with the mechanism of disease [4]. Approximate entropy (ApEn) was considered to provide a measurement of feedback and regularity, and a time series containing many repetitive patterns has relatively low ApEn, and a less predictable process has higher ApEn [5]. Since it has been found that the underlying mechanisms involved in the control of the FHR are mainly nonlinear [4], several studies have presented the use of nonlinear analyses to characterize the presence of nonlinear features in FHR variability [6–9]. Li et al. [9] suggested that the lower ApEn of FHR was associated not only with fetal distress and hypoxia, but also with respiratory and metabolic acidosis in women at term pregnancy.

During labor, fetuses suffer considerable stress due to uterine contraction, repeated circulation insufficiency and resultant hypoxic environment, and head compression in the passage through the pelvic cavity. However, labor does not appear to impair fetal well being significantly, maybe due to a fetal compensation mechanism to stress. For intrapartum FHR monitoring, it is essential to understand the normal pattern of the nervous system regulating the stability of cardinal rhythm under such conditions of physiologic stress during labor. The accurate interpretation of the FHR signal according to labor progression may reduce unnecessary cesarean delivery and improve perinatal

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http://dx.doi.org/10.1016/j.earlhumdev.2013.12.007

morbidity and mortality. However, there have been few studies that evaluate the fetus in each labor stage quantitatively. Most of studies that used linear and nonlinear parameters of FHR variability for fetal monitoring focused on fetuses in specific stages of labor, and did not analyze those parameters according to the stages of labor [5–8].

Thus, this study was conducted to see whether the entropy indices of FHR are significantly different according to labor progression. For this purpose, we compared the entropy indices of FHR in fetuses at different stages of labor using FHR recordings just before delivery of fetuses who were delivered in three different modes: vaginal delivery in the second stage of labor, emergency cesarean delivery in the middle of the first stage of labor, and planned cesarean delivery in pre-labor. The results of this study are expected to be useful for understanding the characteristics of the cortical nervous controlling system of FHR with labor progression and for improving the clinical application of entropy indices for intrapartum fetal monitoring.

2. Materials and methods

We analyzed the stored and digitalized FHR recordings of external cardiotocography measured before delivery at a tertiary hospital. Between August 2004 and December 2006, consecutive cases of vaginal delivery were enrolled. Also, between June 2006 and December 2006, consecutive cases of cesarean delivery, both elective and emergency, were enrolled. Elective cesareans were performed in pre-labor and emergency cesareans were performed in the first stage of labor with an indication of dystocia. Cesarean deliveries with an indication of fetal distress were excluded in this study. Among deliveries of singleton fetuses >37 weeks of gestation, we included fetuses with at least a half an hour of records of cardiotocographic fetal monitoring before delivery. Fetuses with intrauterine growth restriction or major congenital anomalies were excluded. As a result, 450 consecutive deliveries were enrolled in this study. After excluding 116 recordings with missing data of a large segment over 15%, finally, all 334 recordings were included for this analysis. Based on delivery modes and stages of labor, all recordings were divided into 3 groups: recordings in the second stage of labor before vaginal delivery, recordings in the middle of the first stage of labor before emergency cesarean delivery, and recordings in the pre-labor before elective cesarean delivery. There were 280, 31, and 23 recordings in the vaginal delivery group, emergency cesarean group, and elective cesarean group, respectively. This study was approved by the Institutional Review Board of the Catholic University of Korea.

2.1. Signal acquisition and pre-processing

For FHR signal acquisition, a Corometrics 150 (Corometrics, CT, USA), and a Doppler ultrasound cardiotocography with an autocorrelation function were used. Pulse repetition frequency of 2 Hz, pulse duration of 92 μs, and heart rate counting range of 50–210 bpm were used. All records were stored in the linked personal computer for further off-line analysis. We digitalized the FHR recordings of the last 30 min before delivery of the study group through the Catholic computer-assisted obstetric diagnosis system (CCAOD; DoBe Tech, Seoul, Korea).

FHR signals measured during the last minutes of delivery are likely to be lost or contaminated. A previously published pre-processing algorithm [10] was utilized for signal pre-processing. Heart beats lower than 60 beats per minute (bpm) and beat-to-beat differences of higher than 25 bpm were identified and filtered. Spline interpolation was utilized to substitute for the filtered beats for periods of signal loss of 2 s or less. Longer periods were replaced with the most recent segment of equal length with no signal loss. Finally, all heart rate data in bpm were converted into RR intervals for entropy calculations. Heart rate (bpm) can be expressed as 60/RR interval (second) [11,12].

2.2. Entropy analysis

Approximate entropy (ApEn) quantifies the complexity of FHR variability. Low ApEn values correspond to lower complexity while higher ApEn indicates higher complexity. All mathematical equations have been described in detail elsewhere [3,6]. Briefly, the algorithms are summarized as follows.

A time series of size (i.e. the number of RR in the input sequence) N,

$$x = x_1, x_2, \ldots\ldots x_N.$$

We select an embedding dimension m (sometimes also referred in the literature as pattern length) and we construct a new vector series:

$$\vec{x} = \vec{x}_1, \vec{x}_2, \ldots\ldots \vec{x}_{N-m+1}$$

where

$$\vec{x}_i = \left[x_i, x_{i+1}, x_{i+2}\ldots\ldots x_{i+m-1}\right].$$

The size of the new time series $\vec{x}$ is N − m + 1 and the size of each vector is m. We also select a threshold distance or comparison length r. The distance of two vectors $\vec{x}_i$ and $\vec{x}_j$ of size m is smaller than r when:

$$\left|x_{i+k} - x_{j+k}\right| < r \qquad 0 \le k \le m-1$$

in which case we consider the vectors to be similar.

Given the distance r, the probability of a vector $\vec{x}_i$ of size m of being similar with a vector $\vec{x}_j$ of the same size is

$$C_i^m(r) = \frac{\sum_{j=1}^{N-m+1} \Theta(i,j,m,r)}{N-m+1}$$

$$\Theta(i,j,m,r) = \begin{cases} 1 & \left|x_{i+k} - x_{j+k}\right| < r \\ 0 & \text{Otherwise} \end{cases}$$

We define as

$$\Phi^m(r) = \frac{\sum_{i=1}^{N-m+1} \ln C_i^m(r)}{N-m+1}.$$

The approximate entropy is expressed as

$$\mathrm{ApEn}(m,r,N) = \Phi^m(r) - \Phi^{m+1}(r)c.$$

As explained in the algorithms, three parameters were used in computing the ApEn value: the embedding dimension (m), the comparison length (r), and the number of RR in the input sequence (N). One of the disadvantages in ApEn is that ApEn depends on the number of input sequences. Additionally, the value of 1000 input sequences has been suggested to be sufficient for statistical validity with $m = 2$ and r ranging from 0.1 to 0.2 (i.e. 10% to 20% of the standard deviation (STD) of the input sequence, RR) [3]. The number of RR intervals as input sequence was 2000 in this study. The embedding dimension (m) was empirically set to 2 and the comparison length (r) was calculated for each data as 15% of the STD (i.e. r = 0.15) of RR intervals [3]. In order to confirm our ApEn calculations, another nonlinear measure, SampEn (Sample Entropy), was provided and compared with the results of ApEn. The algorithm of SampEn has been explained in detail elsewhere [13]. As mentioned earlier, in ApEn calculations, a pre-processing algorithm based on previous studies was implemented on the FHR signals, with conversion to RR intervals [12]. The final 2000 consecutive RR intervals (16.7 min), the initial 600 consecutive RR intervals (5 min) of the 2000