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Changes in spectral power of fetal heart rate variability in small-for-gestational-age fetuses are associated with fetal sex

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ABSTRACT

Background: Little is known about the influences of fetal weight and sex on spectral analysis of fetal heart rate (FHR) variability.
Aim: The study aims to assess whether there are differences in spectral power of FHR variability according to fetal weight and sex during labor.
Study design: Case–control study. A total of 414 singleton term deliveries without fetal acidemia were divided into small-for-gestational-age (SGA) (n = 29) and non-SGA (n = 385) groups. Analyses were performed separately according to fetal sex.
Subjects: FHR recordings obtained with cardiotocography during the last 2 h of labor preceding delivery.
Outcome measures: Our outcome measures include spectral power of FHR variability.
Results: For the male group, SGA fetuses had significantly lower values for low, movement, high, and total frequencies of spectral power compared with non-SGA fetuses (all $P < 0.005$). Normalized low frequency (LFn) was significantly higher, and normalized high frequency (HFn) was significantly lower in SGA fetuses compared with non-SGA fetuses (all $P < 0.005$). In contrast, for the female group, there were no significant differences in any of the indices of spectral power between the SGA and non-SGA fetuses. In addition, SGA males had significantly higher LFn spectral power and lower HFn spectral power compared to SGA females ($P = 0.016$, and 0.041, respectively).
Conclusions: SGA males have decreased spectral power of FHR variability compared with non-SGA males during labor. However, there are no differences between SGA and non-SGA female fetuses. It is important in the clinical setting to take fetal weight and sex into account during FHR monitoring using spectral analysis.

1. Introduction

Visual interpretation of fetal heart rate (FHR) tracing is subjective and inter-and intra-observer variations in interpretation are unacceptably high [1,2]. Additionally, it is nearly impossible to give consistent evaluations with visual interpretation since FHR patterns result from very complex physical mechanisms. As a result, effort must be made to objectively detect and quantify FHR variability.

Recently, the spectral power of FHR variability has been reported as a possible objective marker for predicting fetal asphyxia [3,4]. The human brain modulates FHR via interplay between sympathetic and parasympathetic pathways, which is in turn reflected in FHR variability [5]. Generally, the power spectrum of heart rate variations can be quantified by means of mathematical algorithms in low frequency (LF), movement frequency (MF), and high frequency (HF) ranges. The LF range is influenced by combined sympathetic and parasympathetic nervous system fluctuation, while the HF range is primarily controlled by parasympathetic influences [6]. The MF range is associated with fetal movements and maternal breathing. The ratio of the LF and HF powers (LF/HF) provides a marker of sympathovagal balance in the control of heart rate [6].

The power spectral analysis of FHR variability can be influenced by various fetal conditions such as gestational age, fetal activity, and fetal sex [7–9]. Term fetuses have higher LF and HF spectral powers than preterm fetuses [7], and spectral power increases more during fetal activity than during quiet sleep [8]. Fetal sex also appears to influence FHR variability, although conflicting results have been reported [9–14]. Thus, it is possible for fetal weight to influence the spectral power of FHR variability, though few reports have been published on this topic to date. [15]. Consequently, in this study, we assessed whether there are differences in spectral power of FHR variability between small-for-gestational-age (SGA) and non-SGA fetuses. We also examined whether the spectral power changed according to fetal weight increases in non-SGA fetuses. Additionally, analyses were carried out with respect to fetal sex in order to investigate the influence of gender.

The results of this study will be helpful in increasing the accuracy of FHR monitoring by clarifying the FHR variability in SGA fetuses

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compared with non-SGA fetuses. In addition, our data will provide insight into how FHR variability changes according to the sex of the fetus.

2. Materials and methods

We analyzed the stored and digitalized FHR recordings of external cardiotocography measured throughout the intrapartum course of deliveries at a tertiary care teaching hospital between June 2004 and December 2006. Among singleton fetuses ≥37 weeks of gestation, we included those that had available records of cardiotocographic fetal monitoring for the last 2 h of labor preceding delivery, umbilical arterial pH values at birth of ≥7.20, and 5-minute Apgar score ≥ 7. Fetuses with major congenital anomalies were excluded from this study. Additionally, we excluded 23 fetuses with missing data of a large segment over 20%. In all, a total of 414 cases were included in the study groups. All fetuses were divided into male and female groups and were then regrouped based on their birth weight percentiles into the SGA group (birth weights < the 10th percentile), and the non-SGA group (birth weights ≥ the 10th percentile). Birth weights were transformed into percentiles using the Korean gender-specific reference percentiles of birth weight at each gestational age. Gestational age was determined by the measurement of the fetal crown-rump-length on the first-trimester scan. The characteristics of the deliveries and newborn outcomes were collected from the medical records. This study was approved by the Institutional Review Board of the Catholic University of Korea.

For FHR signal acquisition, a Corometrics 150 (Corometrics, CT, USA), a Doppler ultrasound cardiotocography with autocorrelation function was used. Using the autocorrelation function, the demodulated Doppler signal of a heartbeat was compared with the next one and then, the distance between two points of the highest similarity was used to calculate the actual heart period. Pulse repetition frequency of 2 kHz, pulse duration of 92 μs, and heart rate counting range of 50−210 beats per minute (bpm) were used. FHR signals were acquired and stored at a sample rate of 2 Hz in the linked personal computer installed with the Catholic computer-assisted obstetric diagnosis system (CCAOD; DoBe Tech, Seoul, Korea). We digitalized the FHR recordings for the 2 h of labor preceding delivery.

To prevent influences of incorrect heart rates, we selected the intervals that did not have missing data, and if a heart rate value exceeds a certain range (50–210 bpm) or strongly deviated from a set of preceding and successive heart rate values, it is substituted by interpolation. For spectral analysis, the data were re-sampled around the vicinity of 2 Hz and 256-point Fast Fourier transformation was computed [16]. The signal was multiplied by a Parzen window function to reduce spectral leakage [17], and the Fourier transform were calculated. Following frequency bands were chosen: total frequency at 0.04–1.00 Hz, LF at 0.04–0.15 Hz, MF at 0.15–0.50 Hz and HF at 0.50–1.00 Hz [6]. To minimize the effects of the changes in total power on the LF and HF component values, normalized LF (LFn) and normalized HF (HFn) powers were calculated by dividing LF and HF powers, respectively, by total power. We also calculated LF/HF to demonstrate the balance of sympathetic and parasympathetic control [6]. The values of spectral power are given in arbitrary units (A.U.).

For statistical analyses, we compared mean FHR, standard deviation of FHR, and spectral indices of FHR between the SGA group and the non-SGA groups using the Mann–Whitney *U* test, for both male and female fetuses. Fetal and maternal characteristics were compared using the Student *t*-test. Furthermore, we carried out male–female comparisons for all indices of spectral power in the SGA and non-SGA groups, using the Mann–Whitney *U* test. To determine whether there were differences in spectral power according to fetal weight increases among the non-SGA fetuses, we performed a Spearman correlation analysis between fetal weight percentiles and spectral powers of FHR variability in the non-SGA male and female subgroups. A *P*-value of less than 0.05 indicated a statistical significance. The Statistical Package for Social Science Software (version 12.0; SPSS, Chicago, IL, USA) was used.

3. Results

A total of 216 male and 198 female fetuses were included in this study. The mean birth weight was 3297.1 ± 392.9 g. Of the 414 fetuses, 29 were SGA (7.0%), and 385 (93.0%) were non-SGA fetuses. the mean FHR was 140.1 ± 9.0 bpm and the total frequency spectral power at 2 h preceding delivery averaged 0.0160 ± 0.0119 A.U. The baseline characteristics of the deliveries and newborn outcomes are shown in Table 1.

The mean FHR and spectral power of FHR variability were compared between the SGA group and non-SGA groups according to fetal sex (Table 2). For female fetuses, there were no significant differences in any of the indices of FHR variability between the SGA and non-SGA groups, whereas for male fetuses, LF, MF, HF, and total frequency spectral powers were significantly lower in the SGA group relative to the non-SGA group ($P = 0.049$, 0.005, 0.002, and 0.039, respectively). As for the indices that depict the balance between the two branches of the autonomic nervous system, LFn and LF/HF values were significantly increased in SGA males compared with non-SGA males ($P = 0.002$ and 0.011, respectively), and HFn values were significantly decreased in SGA males ($P = 0.015$).

As shown in Fig. 1, when spectral indices of FHR for male and female fetuses in the SGA groups were compared, LFn spectral power was significantly higher in male compared with female fetuses ($P = 0.016$), but HF and HFn spectral power was significantly lower in male than in female fetuses ($P = 0.046$ and 0.041). LF, MF, and total frequency spectral powers showed no differences in male–female comparisons in the SGA group. In contrast, in the non-SGA group, there were no significant differences between male and female fetuses in spectral power of FHR variability over all frequency bands including LF, MF, HF, total frequency, LFn, and HFn ($P = 0.663$, 0.648, 0.776, 0.684, 0.875 and 0.229 respectively).

Additionally, there was no significant correlation of changes in fetal weight percentile and spectral power of FHR variability within the non-SGA group, for either gender (Table 3).

4. Discussion

This study showed that SGA male fetuses have lower spectral power of FHR than non-SGA male fetuses during the 2 h of labor preceding delivery. This phenomenon was not, however, observed in female fetuses.

Table 1
The baseline characteristics of the deliveries and newborn outcomes.

Characteristics	Total (n = 414)
Maternal age (years)	31.2 ± 3.5
Gestational age (wk)	39.7 ± 1.1
Parity (nulliparity)	287 (69.3%)
Birth weight (g)	3297.1 ± 392.9
Birth weight percentile	
<the 10th percentile	29 (7.0%)
the 10–90th percentile	353 (85.3%)
≥the 90th percentile	32 (7.7%)
Fetal gender (male)	216 (52.2%)
Apgar score	
1 min ≥ 7	403 (97.3%)
5 min ≥ 7	414 (100.0%)
Umbilical arterial blood pH	7.368 ± 0.068
Umbilical arterial blood HCO3	12.9 ± 11.9
Mean FHR (bpm)[a]	140.1 ± 9.0
Standard deviation of FHR (bpm)[a]	9.1 ± 3.2
Total frequency spectral power of FHR ($\times 10^{-3}$) (A.U.)[a]	16.03 ± 11.18

All values are expressed as mean (± standard deviation) or number (%).
FHR; fetal heart rate.
[a] During the last 2 h of labor preceding delivery.