Technology and Health Care 24 (2016) S471–S476
DOI 10.3233/THC-161170
IOS Press

Influence of gestational age and time of day in baseline and heart rate variation of fetuses

Guangfei Li[a], Song Zhang[a], Lin Yang[a,*], Shufang Li[b], Yan Wang[b], Dongmei Hao[a], Yimin Yang[a], Xuwen Li[a], Lei Zhang[c] and Mingzhou Xu[d]
[a]*College of Life Science and Bio-engineering, Beijing University of Technology, Beijing, China*
[b]*Obstetrics and Gynecology, Peking University Third Hospital, Beijing, China*
[c]*Beijing Yes Medical Devices Co., Ltd., Beijing, China*
[d]*Beijing Aerospace ChangFeng Co., Ltd., Beijing, China*

Abstract.
BACKGROUND: Fetal electrocardiography (FECG) places electrodes on the maternal abdomen to convert the fetal electrocardiosignals into fetal heart rate (FHR), improving the accuracy and comfort of pregnant woman. At the same time, FECG simplifies the procedure of long term monitoring in the perinatal period.
OBJECTIVE: Investigating the influence of gestational age and time of day on FHR features to distinguish between non-stress test (NST) normal fetuses and NST suspicious fetuses.
METHODS: A novel method of FHR baseline estimation was presented; then baseline value and fetal heart rate variation (FHRV) were analyzed in the time domain using FHR signals recorded from 52 fetuses.
RESULTS: Baseline values in 1:00, 2:00, 4:00, 5:00 and heart rate variation (HRV) distribution showed a significant difference ($p < 0.05$) between NST normal fetuses and NST suspicious fetuses.
CONCLUSIONS: The results suggest that NST normal and suspicious fetuses had same outcome and different FHR features. Accurately distinguishing normal fetuses and suspicious fetuses is important for lowering the false positive rate and reducing unnecessary clinical intervention.

Keywords: Fetal heart rate (FHR), baseline, heart rate variation (HRV), gestational age (GA)

1. Introduction

Cardiotocography (CTG) is a common method of fetal surveillance worldwide that can obtain objective data [1]. The NST diagnoses fetal status by adopting Doppler ultrasound to obtain a CTG graphic in the clinic. The NST duration was usually 20 or 40 minutes, and the maximum duration was no more than 1 hour. Many suspicious fetuses' Apgar scores and outcomes are the same as the NST normal ones'; in addition, the 20 or 40 minutes of data may occur during the fetus' quiet sleep cycles, which may lead to some normal fetuses being wrongly diagnosed. In our study, we use the FECG monitor to acquire FHR signals whose lengths are over 10 hours to explore more comprehensive information.

The FHR baseline is an imaginary line changing over time. Fetal baseline variation is the result of the interaction between the sympathetic nerve and the vagus nerve. The sympathetic nerve and the vagus nerve continuously coordinate, producing different instant fetal heart rates, which are reflected in the

*Corresponding author: Lin Yang, College of Life Science and Bio-engineering, Beijing University of Technology, Beijing, China. Tel.: +86 17091081228; E-mail: yanglin@bjut.edu.cn.

Table 1
The basic information of mothers

Index	Age	Monitor time	Signal lost	Valid time
Normal	30.75 ± 2.79	17.85 ± 4.49	10.91% ± 9.49%	15.81 ± 4.14
Suspicious	31.87 ± 4.20	16.81 ± 5.04	6.85% ± 7.26%	15.57 ± 4.76
P-value	0.317	0.471	0.108	0.860

FECG by the fetal baseline variation. Interpretation of fetal HRV is the basic diagnostic tool in present-day perinatal medicine [2]. Fetal HRV has been considered the most useful indicator of fetal well-being antepartum [3].

This study analyzes the baseline's change trend and distribution of the HRV values. Then we use them to analyze the recordings of normal fetuses and suspicious fetuses.

2. Methods and materials

2.1. Subjects

Fifty-two antepartum FECG recordings, derived from abdominal electrocardiograms (ECGa), were recruited for the study. The subjects' GA range was between 30 weeks to 41 weeks. Table 1 shows basic information about the mothers. Valid time means the length of valid signals. All of the subjects were singleton and none had known adverse outcomes. All the fetuses' Apgar scores were 10-10-10. All basic information between the two groups had no significant differences. The study had the approval of the Ethical Committee of Peking University Third Hospital, and all subjects signed an informed consent before enrolling.

2.2. Signal acquisition

The FHR signals were recorded by a FECG monitor (Monica AN24) during the antepartum period. The recording was in a csv format file that was acquired by a monitor machine, and the FHR signal value which was not detected was 0 beats per minute (bpm). The reason for the FHR signal not being detected is that the electrode slice became loose or the signal was masked by noise. The average recording duration was 18.43 hours. The recording lost rate was the ratio of the number of 0 bpm to the number of the FHR value in this recording. Each subject's recording lost rate was lower than 30%, and each recording length was longer than 10 hours. The average valid recording length was 16.68 hours.

All the subjects were divided into two groups according to the NST. The NST observed fetal heart rate changes after fetal movement without external load or uterine contraction stimulus. Usually, there were at least three or more instances of fetal movement; FHR acceleration in 20 minutes was referred to the NST reactive type. The NST can be divided into three types: reactive type, suspicious type and no response type. 26 subjects' NSTs in our study were the reactive type as part of the normal group, and the other 26 subjects' NST were the suspicious type as part of the suspicious group.

2.3. Baseline estimation

The first and the main step in FHR trace analysis is an estimation of the FHR baseline [4]. The baseline can be used to recognize other characteristic patterns like accelerations and decelerations remaining in strict correlation to the fetal state [5]. The International Federation of Gynecology and Obstetrics (FIGO)

has defined the baseline as a mean level of the FHR when it is stable, with acceleration and deceleration absent. It is determined over a time period of 5 or 10 minutes and expressed in bpm. After acquiring the FHR signals, the stage of baseline value extraction follows.

The algorithm includes three main steps. After inputting the FHR signals, the first step is detecting signals, in which the signal is split in 10 minute-long pieces. Because a length of 10 minutes is needed to calculate FHR baseline, pieces with durations of less than 7 minutes were rejected to ensure a lost rate lower than 30%. The rest of the pieces were taken as valid signals. For the second step, the valid signal was divided into sequences, where one length was 1 minute. Then the valid signal folded as matrix (A), which is shown in Eq. (1). Matrix (A) contains M sequences and the number of 10-minute pieces is (M-9), namely the valid signal's length is M minutes. In matrix (A), d(i) indicates a piece of valid signal that has a length of 1 minute. As a baseline value requires 10 minutes of signals for extraction, matrix (A) helps us obtain the baseline value for each 1 minute. In each row of matrix (A), meaning 10 minutes of signal, traverse to get an appropriate FHR value (b), meeting the requirement that we could find the most valid FHR values in the range of $b-5$ to $b+5$. The progress like scanning the FHR values' distribution from lowest FHR to highest FHR with a scanning bandwidth was 10 bpm ($b-5$ to $b+5$); the bandwidth of value (b) covered most of the FHR values. The number of the most valid FHR values should be larger than 480 (480 was the number of FHR values that 2 minutes of signals contain). So far, we determined that each 1-minute signal possesses a baseline value, and then we needed to interpolate value to make sure that the baseline's length was the same as the signal's length. To obtain the final estimation of the baseline, on the third step, all the appropriate FHR values underwent average optimization and cubic spline interpolation. Then, we got the baseline value.

$$A = \begin{bmatrix} d(1) & d(2) & \cdots & d(9) & d(10) \\ d(2) & d(3) & \cdots & d(10) & d(11) \\ \vdots & \vdots & & \vdots & \vdots \\ d(M-10) & d(M-9) & \cdots & d(M-2) & d(M-1) \\ d(M-9) & d(M-8) & \cdots & d(M-1) & d(M) \end{bmatrix}_{(M-9)\times 10} \tag{1}$$

2.4. FHR analysis

Through the short-range monitoring analysis of 4412 cases that had healthy pregnant outcomes in 2009, Serra and his colleagues found that the baseline of FHR continuously declined with the increase of GA from 25 weeks to 41 weeks [1]. Matrix (A) contained (M-9) rows and 10 columns; each row means 10-minutes of signals, and in each row we can extract a baseline value. For example, in the first row, which expressed the 1^{st} minute to the 10^{th} minute, we can obtain a baseline value of the 1^{st} minute. Then we can extract a baseline value per minute. We extracted a baseline value per minute, and then calculated the average per hour. In Eq. (2), BL(i) represents the baseline value of i^{th} minute; as N was 60, then mBL was the average of the baseline value in an hour.

After acquiring the FHR baseline values, the next step was extracting the FHR features. The features in the time domain that we employed have already been used with reasonable success in the antepartum case [6]. We decided to use features in the third trimester, as the difference in variation between the active and quiet cycles or states becomes more marked with advancing gestation [7]. The features employed were the following:

Mean value of the baseline (BL) value:

$$mBL = \frac{1}{N}\sum_{i=1}^{N} BL(i) \tag{2}$$

Table 2
The comparison of HRV tercile in GA

	Normal	Suspicious	P-value
5%	1.7 ± 0.3	1.3 ± 0.2	$< 0.001^*$
25%	4.3 ± 0.9	3.2 ± 0.6	$< 0.001^*$
50%	6.9 ± 1.6	5.1 ± 1.0	$< 0.001^*$
75%	11.0 ± 2.5	8.1 ± 1.6	$< 0.001^*$
95%	21.4 ± 4.9	17.7 ± 3.1	0.002^*
Mean	8.7 ± 1.9	6.7 ± 1.1	$< 0.001^*$

*represent p-value < 0.05.

N is the total number of a piece of time samples of the recording. As this was an extended study with 91% of the recordings longer than 11 hours, N was set to 60, which stands for 1 hour's signal.

Standard deviation of baseline value:

$$SD = \sqrt{\frac{1}{N-1}\sum_{i=1}^{N}(BL(i) - mean)^2} \tag{3}$$

Heart rate variation (HRV):

$$HRV = \max_{i\in[1,T]}(FHR(i)) - \min_{i\in[1,T]}(FHR(i)) \tag{4}$$

T is the length of short-time. We split the HRV value into three ranges: 0–5 bpm is the small variation (SV), 6–25 bpm is the medium variation (MV) and bigger than 25 bpm is the significant variation or large variation (LV). Through the method of magnetocardiogram, Lang recorded 22 low-risk singleton pregnancy pregnant women's data and discovered that low baselines always correspond with small variation. He also found that there were no significant changes in HRV between 8:00 to 18:00 [8]. The acceleration fragment and deceleration fragment were eliminated before calculating the proportion of HRV range.

2.5. Statistics analysis

First of all, a Gaussian test was performed on the subjects to verify that the related features were normally distributed. Subjects' applied K-S test result showed that the mBL and HRV's p-value were bigger than 0.05, meaning they were normally distributed. Normal distribution was the precondition of an independent-samples T test. Then an independent-samples T test to the normal group vs. the suspicious group was performed. The independent-samples T test helped us explore whether the NST of normal fetuses and the NST of suspicious fetuses had significant difference. Then the correlation between GA and HRV was analyzed. Finally, the differences between the two groups were calculated and compared. All the statistical tests were performed using the SPSS 20.0 software package. A value of $p < 0.05$ was considered statistically significant.

3. Results

The baseline value declined with the maturity of fetuses in the third trimester. In this study, we found that the baseline value had a falling tendency from 22:00 to 2:00. At the same time, the value of the baseline in the normal group was higher than in the suspicious group, which is shown in Fig. 1. There was a significant difference between the two groups' baselines in 1:00, 2:00, 4:00 and 5:00.

Table 2 shows that all of the centiles and means of variation in the normal and suspicious fetuses had a strong significant difference ($p < 0.001$).

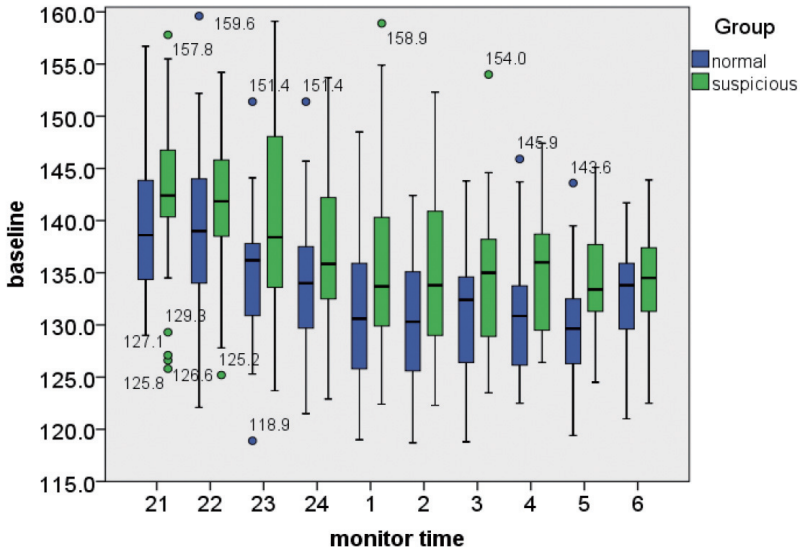

Fig. 1. The baseline trend in day of time.

4. Discussion

The NST has disadvantages: first, different GA and time of day have the same evaluation criteria, despite the fact that fetuses constantly grow with FHR baseline value and HRV changes. Second, the typical NST reaction type and the typical NST abnormal type were definitively judged, but the NST suspicious type did not have a specific criteria.

The mean of the baseline value indicated that the FHR baseline had a downtrend from 22:00 to 5:00, and normal fetuses' baselines were lower than suspicious fetuses' baselines by about 4 bpm from 23:00 to 5:00. In this study, the suspicious fetus' higher baseline values might illustrate that suspicious fetuses are not as mature as normal ones.

HRV was an important feature in studying fetal behavioral states [9]; HRV analysis can help identify stress conditions, as it is sensitive to the autonomic nervous system (ANS) [10]. The number of fetuses was less than 10 per week. The next step is collecting more data to analyze the relationship between the FHR's features and GA. In 2014, Redman used 64 features and three classifiers: linear regression, linear support vector machine (SVM) and radial basis function (RBF) SVM to distinguish fetal acidemia from healthy fetuses; results showed that RBF SVM possesses the best performance [11]. Emina used multi-scale principal component analysis (MSPCA) for noise reduction of electrocardiogram (ECG) signals and autoregressive (AR) modeling for extracting features, achieving 99.93% accuracy of heart beat classification [12]. Results of this study were promising, as our final objective is to identify a set of parameters that could be used as the classifier to improve the accuracy rate of distinguishing normal fetuses from suspicious fetuses.

The outcome between the two groups had no significant difference. But the suspicious fetus' waste of medical resources was much greater than normal ones'. Comprehensive analysis of the differences between the normal group and the suspicious group helped to reduce the waste of medical resources.

5. Conclusion

In conclusion, baseline and the distribution of HRV values in two groups had a significant difference, which reflected that normal fetus developed better than suspicious one. Extending the number of subjects to 30 per GA in different group might help finding a more accurate threshold value to distinguish the normal and suspicious fetuses.

Acknowledgements

This research was partially sponsored by Beijing Natural Science Foundation (7132028) and the New talent project of Beijing university of technology (015000514115007).

References

[1] Serra V, Bellver J, Moulden M and Redman CWG. Computerized analysis of normal fetal heart rate pattern throughout gestation. Ultrasound in Obstetrics & Gynecol. 2009: 34(1): 74-79.
[2] Kupka T, Wrobel J, Jezewski J, Gacek A. Evaluation of Fetal Heart Rate Baseline Estimation Method Using Testing Signals Based on a Statistical Model. EMBS Annual International Conference. New York City, USA. 2006: 28: 3728-3731.
[3] Dawes GS, Moulden M, Redman CWG. Improvements in computerized fetal heart rate analysis antepartum. J Perinat Med. 1996: 24(1): 25-36.
[4] Jezewski J and Wrobel J. Global baseline determination in fetal heart rate records with the identification of local prominent rates. Medical Physics and Biomedical Engineering. 1994: 2: 365-369.
[5] Jezewski J, Horoba K, Gacek A, Wrobel J, Matonia A and Kupka T. Analysis of nonstationarities in fetal heart rate signal: Inconsistency measures of baselines using acceleration/deceleration patterns. Signal Processing and its Applications. 2003: 2(2): 9-12.
[6] Magenes G, Signorini MG and Arduini D. Classification of cardiotocographic records by neural networks Neural Networks. IEEE-INNS-ENNS Int. Joint Conf. on Neural Networks. 2000: 3: 637-641.
[7] Pillai M and James D. The Development of Fetal Heart Rate Patterns During Normal Pregnancy. Obstetrics & Gynecology. 1990: 76(5): 812-816.
[8] Lange DS, Leeuwen PV, Geue D et al. Influence of gestational age, heart rate, gender and time of day on fetal heart rate variability, Medical & Biological Engineering & Computing. 2005: 43(4): 481-486.
[9] Brandle J, Preissl H and Draganova R. Heart rate variability parameters and fetal movement complement fetal behavioral states detection via magnetography. Frontiers in Human Neuroscience. 2015: 9: 1-8.
[10] Lucchini M, Signorini MG and William PF. Multi-parametric Heart Rate Analysis in Premature Babies exposed to Sudden Infant Death Syndrome. Conf Proc IEEE Eng Med Biol Soc. 2014: 6389-6392.
[11] Xu L, Redman CWG and Payne SJ. Feature selection using genetic aigorithms for fetal heart rate analysis. Physiological Measurement. 2014: 35(7): 1357-1371.
[12] Alickovic E and Subasi A. Effect of Multiscale PCA De-noising in ECG beat classification for diagnosis of cardiovascular diseases. Circuits Systems & Signal Processing. 2015: 34(2): 513-533.