General Section

Change of autonomic nervous activity during pregnancy and its modulation of labor assessed by spectral heart rate variability analysis

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Summary

Purpose of Investigation: To elucidate the sequential changes of autonomic nervous activity during pregnancy, we examined heart rate variability on two positions and whether autonomic nervous activity affected duration of labor. *Methods:* Thirty-eight normal pregnant women were studied. Frequency domain parameters (HF, LF, LF/HF ratio) and heart rate were obtained by spectral HRV analysis in the supine and left recumbent position in three trimesters. *Results:* We found HF was significantly higher in early pregnancy, while the LF/HF ratio was significantly higher in late pregnancy. The LF/HF ratio was significantly lower when the left recumbent position was assumed. The LF/HF ratio was significantly higher in the longer labor group of primiparous women. *Conclusion:* Our findings demonstrate that sympathovagal balance shifted progressively from a higher vagal modulation towards a higher sympathetic modulation, and the recumbent position activated vagal activity. It is suggested that increased sympathetic activity in late pregnancy could affect the duration of labor.

Key words: Autonomic nervous activity; Spectral heart rate variability; Frequency domain; Pregnancy; Duration of labor.

Introduction

Pregnancy causes various physical stresses by making dramatic changes. Cardiac output increases 30 to 50% by the end of the 2nd trimester and remains elevated during the 3rd trimester. The increase in cardiac output during pregnancy is influenced by decreased arterial blood pressure and vascular resistance and by increases in circulating estrogen, blood volume, stroke volume, tissue demands for oxygen, maternal weight, and basal metabolic rate. The changes that take place in the cardiovascular system are essential to the well-being of the mother and her baby throughout pregnancy [1].

Neural and hormonal control systems may play an important role in the regulation of homeostasis during pregnancy. Neural control of homeostasis is governed by the autonomic nervous system (ANS) by transmitting fast electrical messages along nerve fibers to the internal organs. The system is divided in two distinct parts, the sympathetic and the parasympathetic, which help regulate the internal environment of the body. General responses of the sympathetic nervous system are activated under emergency situations to make internal adjustments that facilitate an appropriate response by the body. In contrast, the parasympathetic system promotes activities that maintain body function from day to day. Hormones are mainly under the control of the hypothalamus. When these control systems break down due to the physical stresses of pregnancy, the functions are not able to keep the body in a healthy state which may cause complications [2-4].

In the course of the last two decades numerous studies in both animals and human beings have shown a significant relationship between the ANS and cardiovascular mortality, including sudden cardiac death [5, 6]. There are presently various methods available for assessing the status of ANS, which include cardiovascular reflex tests, and biochemical and scintigraphic tests. In recent years, noninvasive techniques based on the electrocardiogram (ECG) have been used as markers of autonomic modulation of the heart. These include heart rate variability (HRV), baroreflex sensitivity, QT interval, and heart rate turbulence, a new method based on fluctuations of sinus rhythm cycle length after a single premature ventricular contraction [7]. Among these techniques, analysis of HRV has emerged as a simple, noninvasive method to evaluate the sympathovagal balance at the sinoatrial level [8, 9]. One of the methods to measure HRV is spectral analysis of the heart rate which was first performed by Sayers [10]. It was subsequently used to document the contributions of the sympathetic, parasympathetic and renin-angiotensin systems to the heart rate power spectrum, which introduced frequency domain analysis as a sensitive, quantitative and noninvasive means for evaluating the integrity of the cardiovascular control system.

A well controlled interaction between the sympathetic and the vagal system is necessary for adapting the cardiovascular system to various hemodynamic needs in physiological states, and for nurturing the fetus during pregnancy [11]. By using spectral HRV analysis, the sequential response of ANS has been demonstrated to shift towards a lower sympathetic and higher vagal modulation in early pregnancy, and to change towards a

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higher sympathetic and lower vagal modulation in late pregnancy. The balance between hemodynamic changes of pregnancy and aortocaval compression was considered as the cause of this biphasic changes in ANS [12, 13]. It is also assumed that ANS is related to uterine contractions, which may cause dysfunctional labor.

However, there is no longitudinal report demonstrating sequential changes in the autonomic nervous activity during pregnancy and the relationship between physical stress and obstetrical factors are poorly understood.

Therefore, we elucidated the longitudinal changes of autonomic nervous activities during pregnancy by using spectral HRV analysis on the supine position and the left recumbent position. Furthermore, whether the ANS affects the duration of labor was examined by using spectral HRV analysis.

Subjects and Methods

Thirty-eight healthy women who came to the Hayashi clinic (a private clinic) in Hyogo Prefecture for prenatal visits from May 2004 to March 2005 were studied, including 16 primiparous women and 22 multiparaous women. All had a singleton fetus with vertex presentation and no cardiopulmonary distress or pregnancy complications. The protocol was approved by the institutional review board at the Hayashi clinic. The purpose and risks of this study were explained to each patient before written informed consent was obtained.

For each woman, an ECG recording was obtained in the 1st, 2nd and 3rd trimester. All examinations and procedures were performed according to the protocol. For assessment of cardiac autonomic function, subjects were asked to refrain from smoking and drinking caffinated beverages two hours before the studies. The studies were performed at 2 pm after a light lunch to avoid the effects of circadian rhythm on HRV. Two positions were assumed in random order by the subjects; the supine and the left recumbent position. After ten minutes of supine rest, ECG recordings (Model FX-7302, Fukudadenshi Inc., Kobe, Japan) were obtained during three minutes of spontaneous respiration. RR interval time series were derived from the ECG with a resolution of 2 ms (Fluclet 4.0, Dainippon Pharmaceutical, Japan). Data were manually edited to remove arrhythmias that could interfere with the analysis. Spectral analysis was performed by autoregressive methods. The low frequency (LF) band was determined to be between 0.04 to 0.15 Hz, and the high frequency (HF) band was defined as between 0.15 to 0.60 Hz. The power of these two spectral analysis components was expressed as ms^2. The ratio between the power of the LF and the HF component (LF/HF ratio) was also calculated. HF is generally defined as a marker of parasympathetic modulation. LF is considered as a marker of both vagal and sympathetic cardiac drive. The LF/HF ratio reflects the sympathovagal balance [14]. The heart rate (HR) was also obtained, as increased HR would be understood as a reflection of sympathetic modulation.

We compared HRV in three trimesters on each position to demonstrate the change of HRV during pregnancy. Furthermore, we analyzed HRV between the supine position and the left recumbent position in each trimester. Gestation weeks on three recording occasions were 14.6 ± 1.4 (mean ± SD) weeks in the 1st trimester, 26.5 ± 3.1 weeks in the 2nd trimester, and 32.1 ± 2.3 weeks in the 3rd trimester.

Primiparous and multiparous women were divided in two groups respectively to analyze HRV on the duration of labor. Primiparous women were divided in two groups based on the medium value which was 713 minutes. Multiparous women were divided in two groups based on 480 minutes (6 hours) which is the average labor time for multiparous women.

The result was displayed as frequencies, percentages, mean and standard deviation (SD). Microsoft Excel and Statcel were used to compare the measures of HRV. For comparison between groups, the Student's t-test and chi-square for independence test were used. Confidence intervals (CI 95%) were calculated. A probability (i.e., p value) of < 0.05 was considered a significant difference.

Results

Thirty-eight pregnant women aged 30.7 ± 4.2 years old were studied. The body mass index (BMI) of pre-pregnancy was 19.7 ± 2.1, and the weight gain during pregnancy was 9.7 ± 3.3 kg. Mean duration of labor time was 570.6 ± 508.4 minutes for all participants and the duration of labor for primiparous women was approximately two times longer than that of multiparous women (Table 1).

Table 1. — *Participant's backgrounds (n = 38).*

Age (yrs.)	30.7 ± 4.2
Parity	
primiparous women	16/38 (42.1%)
multiparous women	22/38 (57.9%)
Prepregnancy BMI (kg/m^2)	19.7 ± 2.1
Weight gain during pregnancy (kg)	9.7 ± 3.3
Mean duration of labor (min)	570.6 ± 508.4
primiparous women (n = 15)	817.3 ± 604.9
multiparous women (n = 20)	385.7 ± 329.9

Figure 1 shows the measures of HRV compared between three trimesters in the supine position. HR was significantly higher in the 2nd and 3rd trimester than in the 1st trimester. HF was significantly higher in the 1st trimester than in the 3rd trimester. LF was significantly lower in the 2nd and the 3rd trimester than in the 1st trimester. The LF/HF ratio was significantly higher in the 2nd and the 3rd trimester than in the 1st trimester.

Figure 2 shows the measures of HRV compared between three trimesters in the left recumbent position. HR was significantly higher in the 2nd and the 3rd trimester than in the 1st trimester. There was no significant difference between trimesters on HF, but it tended to decrease as gestational age increased. LF was significantly higher in the 1st trimester than in the 2nd trimester. There was no significant difference between trimesters on the LF/HF ratio, but it tended to increase as gestational age advanced.

Table 2 shows the measures of HRV compared between the supine position and the left recumbent position in three trimesters. Particularly in the 3rd trimester, HR was higher in the supine position than the left recumbent position, while HF and LF were lower in the supine position than the left recumbent position. The LF/HF ratio was significantly higher in the supine position than the left recumbent position.

Figure 3 shows a comparison of measures of HRV

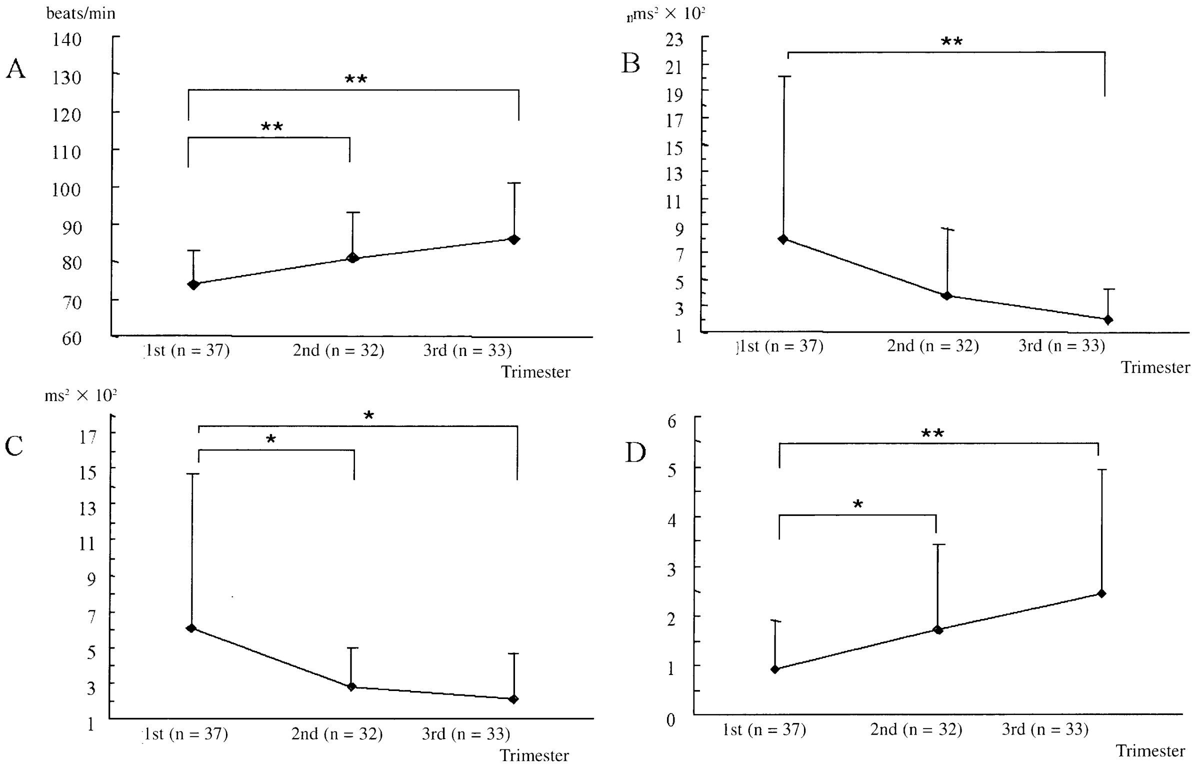

Figure 1. — Comparison of measures of heart rate variability in three trimesters in the supine position. A: HR B: HF C: LF D: LF/HF ratio * $p < 0.05$ ** $p < 0.01$.

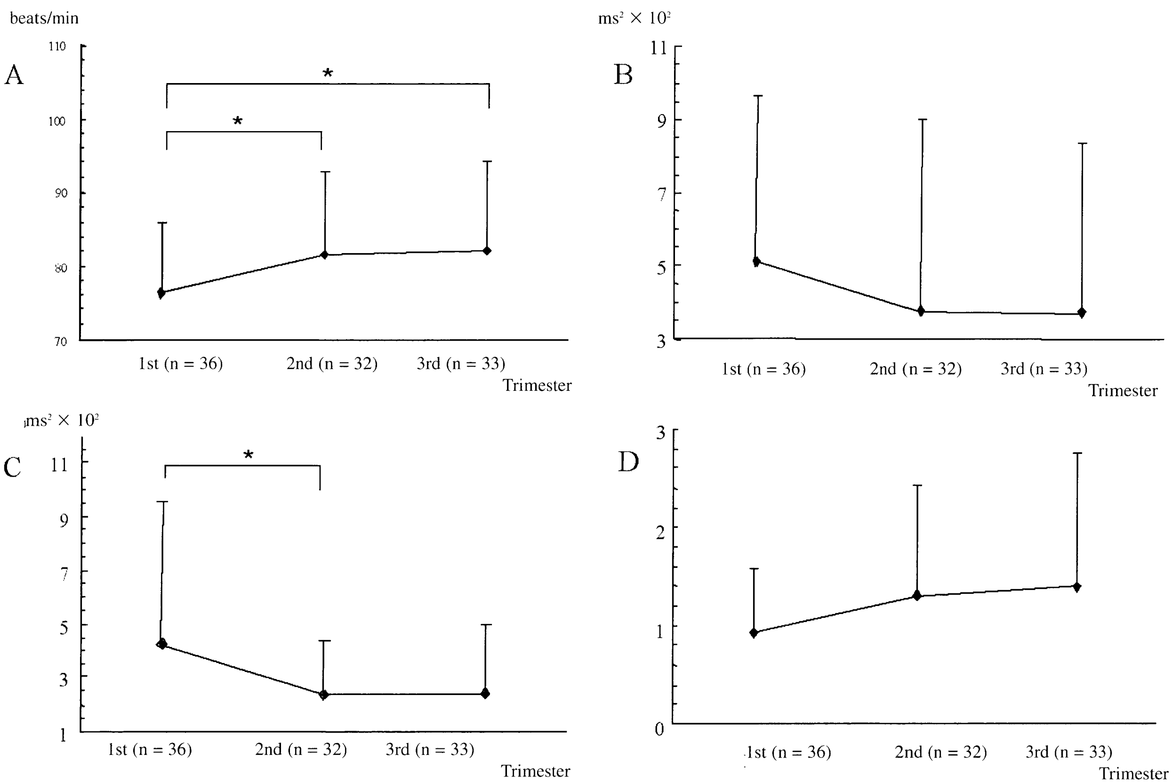

Figure 2. — Comparison of measures of heart rate variability in three trimesters in the left recumbent position. A: HR B: HF C: LF D: LF/HF ratio *$p < 0.05$.

Table 2. — *Measures of heart rate variability compared between the supine position and the left recumbent position in three trimesters.*

	HR	p value	HF	p value	LF	p value	LF/HF ratio	p value
1st trimester								
Supine (n = 37)	73.9 ± 8.8	n.s.	797.4 ± 1214.3	n.s.	602.5 ± 870.7	n.s.	0.9 ± 1.0	n.s.
Recumbent (n = 36)	76.3 ± 9.6		513.2 ± 451.9		425.9 ± 532.4		0.9 ± 0.7	
2nd trimester								
Supine (n = 32)	81.2 ± 11.8	n.s.	375.5 ± 489.7	n.s.	278.2 ± 219.3	n.s.	1.7 ± 1.7	n.s.
Recumbent (n = 32)	81.5 ± 11.2		375.5 ± 521.0		232.0 ± 201.9		1.3 ± 1.1	
3rd trimester								
Supine (n = 33)	86.1 ± 14.9	n.s.	190.2 ± 226.6	n.s.	206.7 ± 258.9	n.s.	2.5 ± 2.5	p < 0.05
Recumbent (n = 33)	82.0 ± 12.0		372.5 ± 460.9		241.6 ± 258.4		1.4 ± 1.4	

n.s.: not significant.

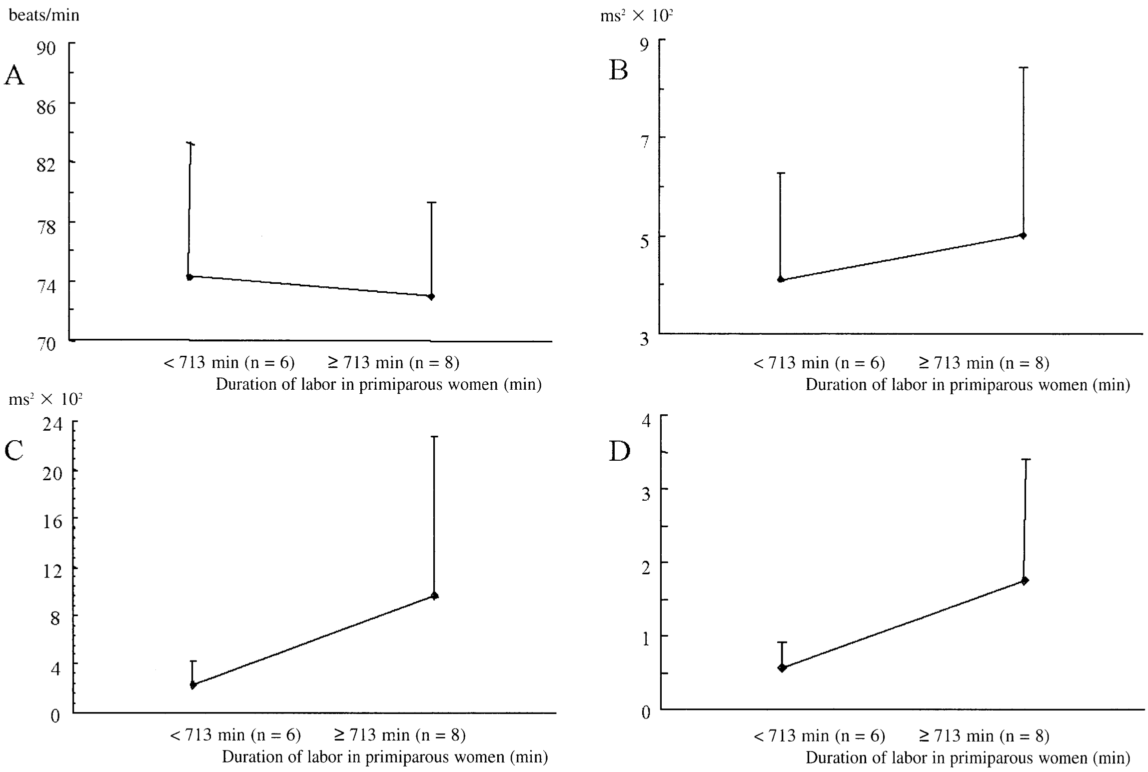

Figure 3. — Comparison of measures of heart rate variability between the shorter labor duration group and the longer labor duration group of primiparous women in the 1st trimester in the supine position. A: HR B: HF C: LF D: LF/HF ratio.

between the shorter labor and the longer labor duration groups of primiparous women in the 1st trimester in the supine position. HR was lower in the longer labor duration group than the shorter labor duration group. HF, LF and the LF/HF ratio were higher in the longer labor duration group than the shorter labor duration group.

Figure 4 shows a comparison of measures of HRV between the shorter and longer labor duration groups of primiparous women in the 2nd trimester in the supine position. HR, LF and the LF/HF ratio were higher in the longer labor duration group than the shorter labor duration group. HF was lower in the longer labor duration group than the shorter labor duration group.

Figure 5 shows a comparison of measures of HRV between the shorter and the longer labor duration groups of primiparous women in the 3rd trimester in the supine position. HR and the LF were higher in the longer than the shorter labor duration group. HF was lower in the longer than the shorter labor duration group. The LF/HF ratio was significantly higher in the longer labor duration group than the shorter labor duration group.

As for multiparous women, we compared the measures of HRV between the shorter and the longer labor duration groups in each trimester in the supine position. There was no significant difference between the shorter labor duration group and the longer labor duration group in any trimester in either position.

Discussion

This is the first time a longitudinal study using spectral HRV analysis has demonstrated that vagal activity was gradually decreased, sympathetic activity was gradually

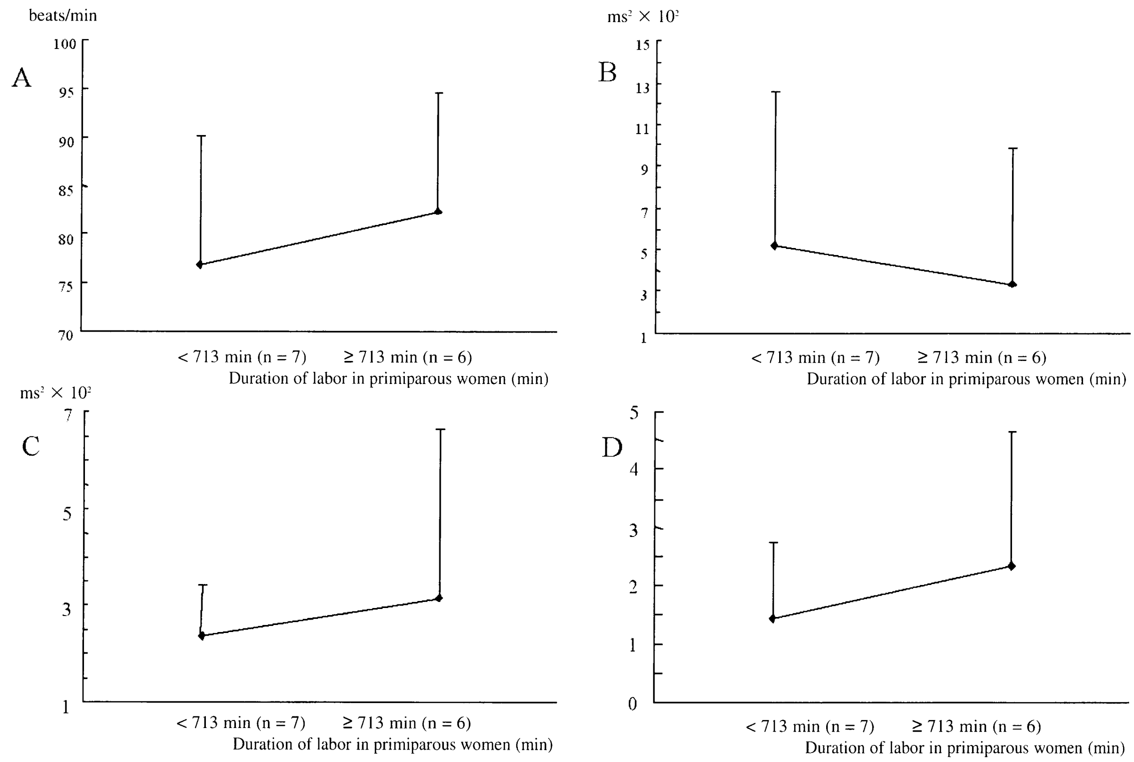

Figure 4. — Comparison of measures of heart rate variability between the shorter labor duration group and the longer labor duration group of primiparous women in the 2nd trimester in the supine position. A: HR B: HF C: LF D: LF/HF ratio.

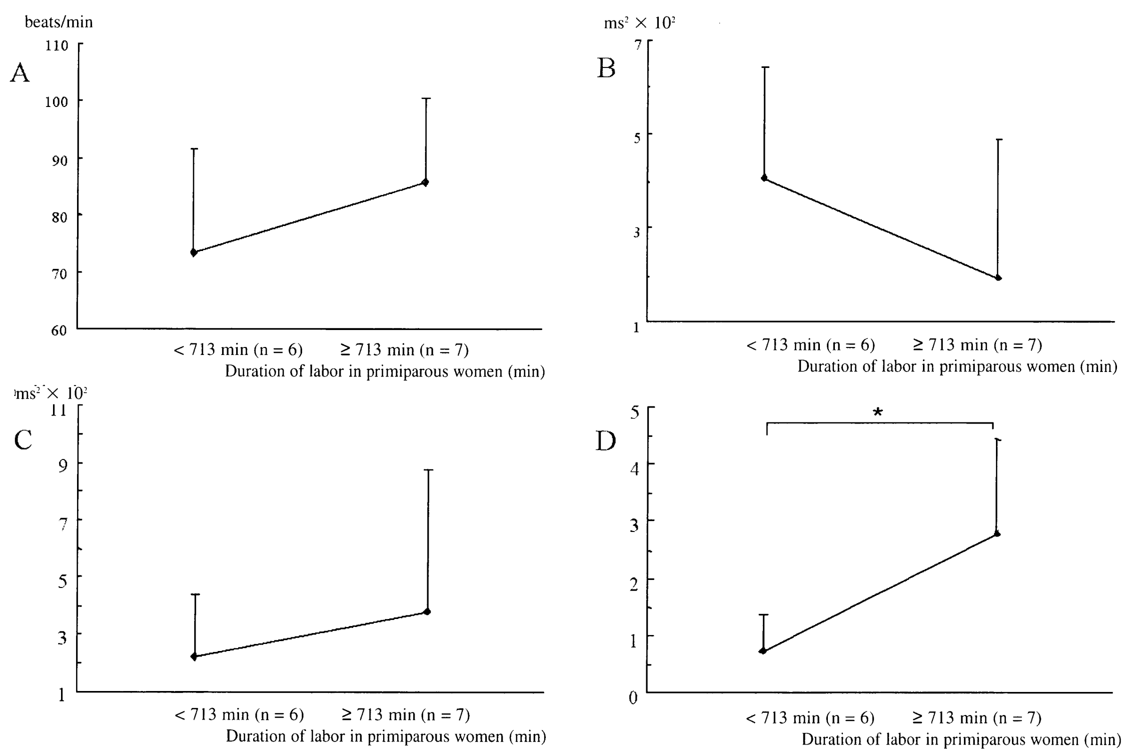

Figure 5. — Comparison of measures of heart rate variability between the shorter labor duration group and the longer labor duration group of primiparous women in the 3rd trimester in the supine position. A: HR B: HF C: LF D: LF/HF ratio $^*p < 0.05$

increased, and the sympathovagal balance shifted from lower sympathetic and higher vagal modulation towards higher sympathetic and lower vagal modulation as gestational age advanced. We also found that these autonomic nervous activities were more apparent in the supine position than the left recumbent position. Kuo *et al.* has reported that cardiac vagal activity is decreased while cardiac sympathetic activity is increased in late pregnancy by using spectral HRV analysis [15]. Ekholm *et al.* has also observed that cardiac vagal activity is decreased during normal midpregnancy as shown by orthostatic provocation, isometric handgrip and deep breathing tests [16]. Our findings were similar to these observations. However, our study revealed longitudinal changes of autonomic nervous activity for adaptation to pregnancy. These changes may be explained by several factors. First, the decline in systemic vascular resistance caused by gestational hormones may reduce the workload of the heart, leading to a lower sympathetic and higher vagal modulation in the 1st trimester of pregnancy. Second, the increase of cardiac output through pregnancy may increase the workload of the heart and consequently shift the autonomic nervous activity into a state of a higher sympathetic and lower vagal modulation as gestational age advances [17, 18]. Third, the endocrine system plays a critical role in the initiation and maintenance of pregnancy. Estrogens and progesterones are essential for these roles and increase vascularity, causing vasodilatation, which helps to nurture the fetus through the placenta, but increases the workload of the heart. Fourth, aortocaval compression would be negligible in late pregnancy. Finally, there may be psychological and mental factors that could influence autonomic nervous activity [12]. Further investigation analyzing the effects of mental factors more specifically are necessary.

Regarding the effect of ANS on the supine hypotensive syndrome, our study indicated the effectiveness of the left recumbent position in the 3rd trimester, since vagal activity was activated and sympathetic activity was decreased when the left recumbent position was assumed. This discrepancy of HRV between the supine position and the left recumbent position could be explained by the loads of venous return and cardiac output [19]. In late pregnancy cardiac output is 22% higher when a pregnant woman is in the lateral recumbent position vs the supine position because the uterus occludes venous return to the heart when she is lying on her back. As a result, cardiac output is decreased and the blood pressure drops rapidly. Symptoms of dizziness, nausea, or diaphoresis when lying on the back indicate that a pregnant woman should turn to her side immediately to relieve compression and restore adequate circulation [1]. Thus, the left recumbent position should be encouraged during pregnancy, since suppression of cardiac vagal activity and enhancement of cardiac sympathetic activity are greater in the supine position and less in the left recumbent position.

As for the effect of ANS on the duration of labor, it was suggested that primiparous women who experienced long labor duration had the sympathovagal balance of a higher sympathetic and lower vagal modulation in the 3rd trimester. The difference between the shorter labor duration group and the longer labor duration group on HR in the 3rd trimester would indicate the big effect of sympathetic activity in late pregnancy. These changes may be explained by the innervation of ANS on the uterus. The nerve supply of the uterus is provided principally by the sympathetic nervous system and partly by the cerebrospinal and parasympathetic systems [20]. The sensory supply of the uterine fundus accompanies the sympathetic fibers to the ganglia of the 11th and 12th thoracic posterior roots. These fibers are believed to carry impulses related to pain. The parasympathetic supply to the uterus comes from the 2nd to the 4th sacral segments. The fibers synapse in the uterovaginal plexus and in the wall of the uterus. A large ganglion on either side of the cervix, the cervical ganglion, contains postganglionic, parasympathetic and some sympathetic neurons. The parasympathetic fibers are accompanied by sensory fibers that supply the cervix and take origin in the sacral ganglia. These fibers carry pain from the cervix which is referred to the sacral region and initiated by dilatation of the cervix. The denervated uterus can function normally during parturition and it is believed that the autonomic nerve supply is mainly concerned with the innervation of blood vessels although terminations of postganglionic fibers on the uterine muscle have been demonstrated [21]. In this context, we suggest that medical care to decrease the physical stress and provide relaxation during pregnancy, especially in the 3rd trimester, may be effective for an easier delivery.

The reason why the comparison of HRV between the shorter labor duration group and the longer labor duration group on multiparous women did not attain statistical significance may be explained mainly by the insufficient numbers of multiparous women. Beyond this reason, it may be explained that the cardiac loads of multiparous women would be less than for primiparous women because the average time of labor is shorter than for primiparous women. At any rate, further studies with larger populations would be needed to consider the effect of ANS on the duration of labor in multiparous women.

In summary, the present study demonstrates that vagal activity was gradually decreased, sympathetic activity was gradually increased, and the sympathovagal balance shifted from lower sympathetic and higher vagal modulation towards higher sympathetic and lower vagal modulation as gestational age advanced. The effectiveness of the left recumbent position in the 3rd trimester was indicated, since vagal activity was activated and sympathetic activity was decreased when the left recumbent position was assumed. It is also suggested that the sympathovagal balance of lower vagal and higher sympathetic activity in the 3rd trimester would affect the duration of labor in primiparous women. Spectral HRV analysis could be recommended as an effective method for assessing the status of autonomic nervous activity during pregnancy and prospecting the duration of labor.

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