INTRAPARTUM FETAL HEART RATE PATTERNS

Quantification and trend detection

FOETALE HARTSLAG PATRONEN TIJDENS DE BARING

Kwantificering en trend-detectie

PROEFSCHRIFT

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I am persuaded that a judicious practitioner will do every thing for the safety of his patients, before he has recourse to any violent method, either with the hand or instrument.

W.Smellie

To my parents and sister.

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LIST OF ABBREVIATIONS

AGA: appropriate-for-gestational age.

bpm: beats per minute.

EFM: electronic intrapartum fetal monitoring.

FHR: fetal heart rate.

phase 1: the one-hour tracing period at 3-5 cm cervical dilation, at least 30 min. after amniotomy.

phase 2: the one-hour tracing period at 7-9 cm cervical dilation, at least 30 min. before the expulsion period.

SGA: small-for-gestational age.

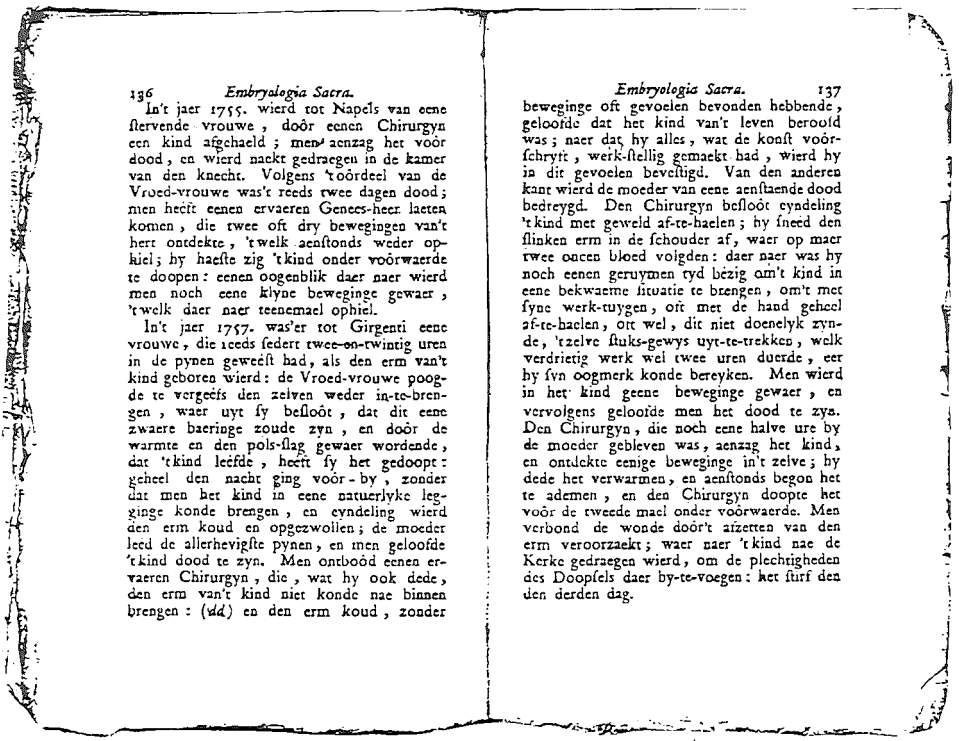
CHAPTER I
GENERAL INTRODUCTION

The clinical benefit of intrapartum fetal heart rate (FHR) monitoring, used to assess fetal condition, is dependent on various factors: 1) an early and reliable detection of fetal distress, 2) the degree to which fetal damage can be prevented by appropriate clinical intervention, and 3) the incidence and severity of maternal and fetal side effects due to the application of the technique, in particular in cases in which no preventable fetal distress is apparent (e.g. most low-risk patients). Fetal monitoring is only of clinical advantage if a group of patients can be identified, in which the benefits of the technique exceed the risks and costs as compared to the use of other methods.

The reliability of the assessment of fetal condition depends on the validity and reproducibility of the methods of analysis of the FHR as well as on the clinical interpretation after analysis. Validity is the extent to which the various aspects of FHR which are analyzed show a sensitive and specific relationship with fetal condition. Reproducibility can be expressed in terms of observer variability, indicating the dissimilarity between different assessments of fetal condition. In this chapter the past and present status of FHR monitoring will be considered with particular attention to its validity and reproducibility. Against this background the scope and design of the studies presented will be defined.

I.1 HISTORY OF THE ASSESSMENT OF FETAL CONDITION BY EVALUATION OF THE FETAL HEART-BEAT.

One of the first descriptions of the assessment of fetal heart action was given by Cangiamila in 1780[1] (Fig.1). Palpable pulsations in a prolapsed fetal arm indicated that the fetus was alive. The unreliability of this sign was shown in the same



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In't jaer 1755. wierd tot Napels van eene ſtervende vrouwe, doôr eenen Chirurgyn een kind afgehaeld; men aenzag het voôr dood, en wierd nackt gedraegen in de kamer van den knecht. Volgens 't voôrdeel van de Vroed-vrouwe was't reeds twee dagen dood; men heeft eenen ervaeren Genees-heer laeten komen, die twee oft dry bewegingen van't hert ontdekte, 't welk aenſtonds weder opkiel; hy haeſte zig 't kind onder voôrwaerde te doopen: eenen oogenblik daer naer wierd men noch eene klyne beweginge gewaer, 't welk daer naer teenemael ophiel.

In't jaer 1757. was'er tot Girgenti eene vrouwe, die reeds ſedert twee-en-twintig uren in de pynen geweeſt had, als den erm van't kind geboren wierd: de Vroed-vrouwe poogde te vergeefs den zelven weder in-te-brengen, waer uyt ſy beſloôt, dat dit eene zwaere baeringe zoude zyn, en doôr de warmte en den pols-ſlag gewaer wordende, dat 't kind leefde, heeft ſy het gedoopt: geheel den nacht ging voôr-by, zonder dat men het kind in eene natuerlyke legginge konde brengen, en eyndeling wierd den erm koud en opgezwollen; de moeder leed de allerheviglſte pynen, en men geloofde 't kind dood te zyn. Men ontboôd eenen ervaeren Chirurgyn, die, wat hy ook dede, den erm van't kind niet konde nae binnen brengen: (dd) en den erm koud, zonder

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beweginge oft gevoelen bevonden hebbende, geloofde dat het kind van't leven beroofd was; naer dat hy alles, wat de konſt voôrſchryft, werk-ſtellig gemaekt had, wierd hy in dit gevoelen beveſtigd. Van den anderen kant wierd de moeder van eene aenſtaende dood bedreygd. Den Chirurgyn beſloôt eyndeling 't kind met geweld af-te-haelen; hy ſneed den ſlinken erm in de ſchouder af, waer op maer twee oncen bloed volgden: daer naer was hy noch eenen geruymen tyd bezig om't kind in eene bekwaeme ſituatie te brengen, om't met ſyne werk-tuygen, oft met de hand geheel af-te-haelen, oft wel, dit niet doenelyk zynde, 't zelve ſtuks-gewys uyt-te-trekken, welk verdrietig werk wel twee uren duerde, eer hy ſyn oogmerk konde bereyken. Men wierd in het kind geene beweginge gewaer, en vervolgens geloofde men het dood te zyn. Den Chirurgyn, die noch eene halve ure by de moeder gebleven was, aenzag het kind, en ontdekte eenige beweginge in't zelve; hy dede het verwarmen, en aenſtonds begon het te ademen, en den Chirurgyn doopte het voôr de tweede mael onder voôrwaerde. Men verbond de wonde doôr't afzetten van den erm veroorzaekt; waer naer 't kind nae de Kerke gedraegen wierd, om de plechtigheden des Doopſels daer by-te-voegen: het ſtarf den den derden dag.

Figure I.1 One of the first descriptions of the assessment of fetal heart action. From: Cangiamila FE. Kort begryp van de embryologia sacra of te verhandelinge der plichten van de priesters, geneesheren, chirugyns en vroedvrouwen, jegens de kinderen die noch niet geboren zyn. Antwerpen: H.Brincken, 1780.

case when, with progress of labor, the arm became cold, swollen, and pulseless, although the infant was born alive. Boerhaave[2] and various German obstetricians[3] at the end of the 18th century used the absence of palpable pulsations in presenting parts (head, foot, or umbilical cord) to confirm fetal death.

Mayor, a surgeon from Geneva, is credited[3] with having been the first to hear fetal heart tones in a near-term fetus in 1818[4], by placing an ear on the abdomen of the mother. Lejumeau[5], viscount of Kergaradec, in 1822 used the stethoscope, introduced a few years earlier by Laennec, and counted the FHR. He recognized the clinical importance of auscultation to determine fetal condition[3]. Kergaradec also investigated influences other than fetal condition on auscultated FHR, such as the position of the fetus and the presence of multiple pregnancy[3]. He counted a lower FHR during labor than antepartum, described acceleration of FHR during a period of excessive fetal movements, and could not demonstrate a relationship between FHR and maternal heart rate[4].

Kennedy[6], as quoted by Goodlin[7], stressed the significance of fetal tachycardia, noted the increased frequency in which FHR irregularities occur in late labor as compared to early labor, and cited a statement by Bodson: "The most ominous FHR pattern is slowness of its return when a contraction is passing on".

These observations were followed by those of Hohl[3] in 1833, who described an elevation of FHR at the beginning of uterine contractions, and also observed decreases in FHR following descent of the fetal chest into the pelvis. He stated that a depressed infant will be born if FHR falls before the descent of the fetal chest, and he stressed the importance of such an event for the decision to perform an operative delivery.

Depaul[8] in 1847 considered repeated bradycardia a sign of fetal distress.

Two years later, in 1849, Kilian[9] developed a more exact

definition, using an FHR below 100 bpm or above 180 bpm as an indication for forceps delivery.

Many years after Kergaradec's first description auscultation of the fetal heart tones came into general use in obstetric practice. At fist, moral objections dominated the literature, leading to discussions concerning the method of auscultation: direct or indirect, on a nude or on a covered abdomen with the women standing or lying down[7,9]. Nevertheless, it appears that the majority of presently recognized FHR patterns and their clinical significance were already described during the first half of the 19th century. However, under the morally restricted conditions of that time, many observers were not able to reproduce the findings of the initial investigators. Even in 1959 there was still no agreement as to which auscultated FHR patterns had to be considered indicative of the presence of fetal distress[10]. As shown by Benson et al.[11] in a prospective study of 24.363 women in labor, there is no reliable single auscultated variable of FHR which is indicative of fetal distress, except when it occurs to an extreme degree. In Benson's study auscultation was started 30 sec. after the end of a uterine contraction, and therefore information must have been missed. Auscultation of FHR has various problems concerning the method of auscultation, observer variation[12,13], clinical interpretation of FHR patterns, and the clinical usefulness of the technique. These problems have not been solved with the introduction of electronic FHR monitoring.

In the early fifties of this century Hon[12] developed the electronic fetal heart rate monitor, based on recording of the fetal electrocardiogram which had already been visualyzed 50 years previously[14]. With the introduction of this electronic technique, a new era of fetal monitoring began.

I.2 PRESENT STATUS OF ELECTRONIC INTRAPARTUM FETAL HEART RATE MONITORING.

Results of prospective clinical trials assessing clinical effects of electronic FHR monitoring (EFM) have raised serious doubts about its clinical benefits. Eight trials comparing EFM with auscultation have been described[15-22]. After four trials it was concluded that in low-risk patients auscultation and EFM were equally acceptable methods of monitoring fetal condition during labor, and that there was no evidence that EFM reduces morbidity and mortality in low-risk pregnancies[23]. Banta and Thacker concluded[24] on the basis of a literature search that the evidence of benefit derived from EFM was contradictory and at best confined to a small decrease in mortality among high-risk patients, in particular concerning low birth weight infants. They concluded that the precision of EFM was low; using the Apgar score as the gold standard, specificity ranged from 44-93%, and sensitivity from 32-84%. These findings and the associated relatively low predictive values of positive and negative tests were considered the reason for the limited clinical benefit of EFM, and for the increased rate of cesarean sections associated with fetal and maternal risk, and with enormous costs. Two large trials[20,22] as well as pooled results of six small trials[25] showed an increase in the frequency of operative deliveries in groups with EFM, and no influence of EFM on perinatal mortality. Only one trial[20] showed a fall in the occurrence of neonatal seizures, but only during the first year of life. In the latter trial it was also suggested that the use of fetal scalp blood sampling may limit the increase in cesarean section rates. However, a recent study indicated that fetal scalp blood sampling is rarely performed in obstetric practice,

even in teaching institutions[26]. FHR tracings of a trial[20] in which scalp blood sampling was performed in 169 fetuses on indication of an abnormal FHR tracing were reviewed retrospectively. The reassessment showed that in 13% of fetuses with FHR tracings judged to require clinical action (usually a fetal blood sample) this action was not taken. However, the method of assessment of FHR tracings and the associated observer variability may have influenced the results of the trial.

I.3 SCOPE AND DESIGN OF THE PRESENT STUDIES.

The present studies were designed and performed to investigate different aspects of the reliability of EFM, including the effects of methodologic changes in the assessment of tracings on the reliability of EFM.

Analysis of FHR patterns. The validity and the relatively low reproducibility[27-29] of FHR assessment may be improved by standardization. To that purpose it was tried to develop a classification of FHR patterns consisting of different sets of criteria applicable to each FHR pattern, exactly defined, mutually exclusive and complementary. For comparibility, such a classification should resemble classifications that were used previously but lacked these characteristics[30-32]. The latter classifications were used in completely visual analyses. It was tried to answer the question as to whether the use of the developed classification and the use of a template in visual analysis further reduce observer variation. Finally it was investigated whether the validity of EFM might be improved by using a standardized duration of the tracings of such a length that unexpected fetal acidosis will probably not occur before the end of the tracing[33] (<120 min.), and the influence of biologic variability of the FHR on the analysis will be limited.

Interpretation of FHR tracings.
Validity of FHR assessment may be improved by exact measurement of various details of FHR
patterns, by determining the trend in the occurrence of FHR patterns during labor[34], and by quantification of FHR patterns. The latter is possible when all patterns are analyzed in tracings with a standardized duration. The use of reference values for the occurrence of FHR patterns may reduce observer variation in FHR interpretation and may increase the validity of an early prediction of fetal distress. For that reason, such values were determined in different phases of the first stage of labor in a clinical study of patients without evidence of obstetric pathology.

Many obstetric factors are known to influence FHR patterns; these influences may partly interfere with or resemble the influence of fetal distress[35,36,37]. Therefore, the relationships between each detail of the FHR patterns measured, the occurrence of fetal distress, and various other obstetric factors were determined.

Specificity, sensitivity and predictive values of standardized and quantitatively assessed FHR patterns were determined in different groups of patients, classified according to the occurrence of obstetric pathology[23], in an attempt to distingiush between patients who may benefit from EFM and those in which the main effects of EFM are fetal or maternal side effects. The standard with which the test results are compared should consist of intrapartum criteria (e.g. fetal scalp blood pH[23]) as well as postpartum criteria (e.g. Apgar score). This will reduce "the fetal monitoring paradox", which indicates that the better the validity of EFM the worse the relationship between intrapartum FHR and postpartum neonatal condition, due to the benefitial effect of intervention.

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CHAPTER II

INTRAPARTUM FETAL HEART RATE PATTERNS I. CLASSIFICATION, QUANTIFICATION, AND OBSERVER VARIATION

II.1 I N T R O D U C T I O N

The assessment of fetal condition using antepartum and intrapartum electronic fetal monitoring contains two important elements: the analysis of fetal heart rate patterns and the clinical interpretation of analyzed data. The reliability of these elements depends on various factors, e.g., observer variability and biologic variability. Many systems have been developed to analyze fetal heart rate patterns[1-3], all using qualitative and visual methods. The use of these methods has resulted in low intra- and inter-observer agreement[4-6] in antepartum as well as in intrapartum cardiotocography.

There are many causes of observer disagreement, such as differences in the interpretation of criteria, omissions in visual pattern recognition, errors in the measurement of variables or in data handling. These factors may be prevented in part by using a standardized method of analysis and objective criteria. For that reason a standardized method of visual analysis and quantitation of variables of intrapartum fetal heart rate variability was developed, and the results of a study of its intra- and inter-observer variation are presented. The effect of the length of the tracing sample on the reproducibility of the analysis was also studied to assess the influence of biologic variability.

II.2 M A T E R I A L A N D M E T H O D S

Intrapartum cardiotocograms recorded in 200 consecutive term patients labeled as being "high risk", were selected for analysis, at the Department of Obstetrics and Gynecology, Ikazia Hospital, Rotterdam. Fetal heart rate, derived from the fetal ECG obtained with a scalp electrode, and intrauterine pressure, measured by means of a fluid-filled open-tipped catheter and a

pressure transducer ,were recorded with a Hewlett-Packard cardiotocograph type 8030 A, at a paper speed of one cm per minute. From each patient a one-hour sample, obtained at a cervical dilation of 4-6 cm, was used for analysis.

SELECTION OF TRACINGS.

The 200 one-hour samples were analyzed visually for the presence or absence of short-term and long-term variability. They were then divided into five subgroups, each containing at least 20 samples with: 1) zero to five accelerations without decelerations, 2) more than five accelerations without decelerations, 3) short-term variability amplitude less than 3 bpm, 4) decelerations without accelerations, 5) decelerations as well as accelerations. Ten samples of each of these five subgroups were then randomly selected and allotted to two groups of tracings which were subsequently used for determination of observer variability.

CLASSIFICATION OF HEART RATE PATTERNS.

The criteria for classification are shown in table II.1, examples in figure II.1, and in Appendix 1.

C o n t r a c t i o n s. Each elevation of the intrauterine pressure curve of 20 mm Hg or more above zero level[7] (air pressure level in labor room) sustained for 10 seconds or more was considered a uterine contraction.

B a s e l i n e f r e q u e n c y. Baseline frequency of the fetal heart rate was defined as the mean heart rate in the absence of long-term variations or uterine contractions[2].

S h o r t - t e r m v a r i a b i l i t y. The short-term variability consists of rapid variations in the fetal heart rate pattern. It was assessed by the oscillation amplitude and defined as the mean amplitude of all variations above and below the baseline frequency with a duration of less than 15 seconds. Oscillation amplitude was determined in the absence of uterine contractions or long-term variability.

TABLE II.1. Classification of fetal heart rate patterns

Variable	Classification criteria
Baseline frequency	classes of 10 bpm* : 70, 80, 90, 100, 110 etc.
Short term variability	
Amplitude V in bpm	A: V<3 B:3<V≤5 C:5<V≤15 D:15<V≤25 E:V>25
Long term variations	
Duration (sec)	A:15-19 B:20-39 C:40-59 D:60-119 E:120-179
Amplitude (bpm)	a:15-19 b:20-29 c:30-39 d:40- 49 e: ≥50
Type	Acc:Acceleration Dec:Deceleration Com:Combination
Relationship to uterine contraction	Acc: contraction- and pause- accelerations Dec: early : lagtime < 10 sec intermediate: lagtime 10-30 sec late : lagtime > 30 sec
Shape	Acc: simple-shape: notch < 10 bpm N-shape : notch ≥ 10 bpm M-shape : notch at baseline Com: AD-shape : consecutive Acc+Dec DA-shape : consecutive Dec+Acc ADA-shape : consecutive Acc+Dec+Acc

* beats per minute

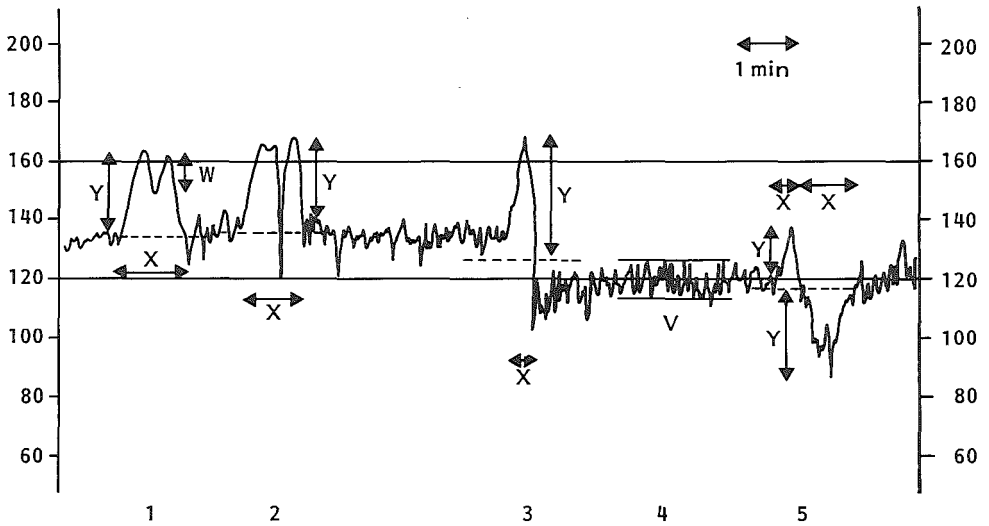

Figure II.1. Fetal heart rate (bpm) tracing. Examples of classification of patterns: 1 = N-shaped acceleration (W = notch-amplitude), 2 = M-shaped acceleration, 3 = simple-shaped acceleration, 4 = short-term variability (V = amplitude), 5 = AD-combination pattern, X = duration, Y = amplitude. Dotted lines indicate the mean baseline frequencies.

L o n g -t e r m v a r i a b i l i t y. In the classification of long-term variations elements of the classifications of Hon[3] and Caldeyro-Barcia[2] were used, with modifications. A long-term variation was defined as a single oscillation or a group of consecutive oscillations each deviating at least 15 beats per minute during at least 15 seconds from the baseline frequency. These variations were classified according to type, duration, amplitude, shape and relationship to uterine contraction.

According to the direction of deviations from the baseline frequency, three types of long-term variations were distinguished: accelerations, decelerations and combination patterns.

To determine the duration of a long-term variation the mean baseline frequency was assessed in a two-minutes segment before (onset baseline frequency) and after (terminal baseline frequency) each variation which exceeded short-term variability. The arithmetic mean of these two frequencies (MBF) was used as the baseline frequency during a long-term variation or a group of subsequent long-term variations. The duration was defined as the time difference between the start of the oscillation which deviated during at least 15 seconds with a maximum amplitude of at least 15 bpm from the onset baseline frequency, and the end of the last oscillation which deviated at least 15 seconds with a maximum amplitude of at least 15 bpm, from the terminal baseline frequency.

The amplitude (bpm) of a long-term variation was determined by the maximum deviation from the MBF during the oscillation or group of oscillations which formed the long-term variation.

The shape of a long-term variation was assessed in accelerations and in combination patterns. Superimposed oscillations were considered part of the same simple acceleration when the separating notch was less than 10 bpm. When the notch reached 10 bpm and the superimposed oscillation itself met the criteria for an acceleration the pattern of

consecutive oscillations was termed an N-acceleration, and when one of the notches reached or passed MBF the pattern was termed an M-acceleration. In combination patterns consecutive deviations from MBF may have different directions; their shape is determined by the order of the variations, all of which are required to meet the criteria for accelerations or decelerations.

The relationship between accelerations and decelerations, and uterine contractions was defined. Accelerations which concur completely or in part with a contraction were termed contraction-accelerations, all other accelerations were called pause-accelerations. The criterion of the lag-time (sec.) between the maximum of the contraction and the maximum deviation from MBF was chosen for decelerations.

QUANTITATIVE ANALYSIS.

Baseline frequency, short-term variability amplitude, and uterine contractions were expressed as their added quantities in each one-hour sample. For long-term variations the total quantity of patterns in each of the 150 classes of accelerations, 75 classes of decelerations and 16,875 classes of combination patterns were calculated in each one-hour sample. The numbers of long-term variations and uterine contractions were expressed as means per ten minutes.

DESIGN OF THE STUDY.

In the first group of 50 tracings about 600 fetal heart rate patterns, including many small variations, were marked and numbered before analysis (type 1 study). Observer A, an experienced obstetrician, and observer B, a resident in obstetrics with limited experience, were asked to classify only numbered variations and to record the reason why a variation was not considered a long-term variation. Using a transparent template with inscribed classes (figure II.2), all variables were determined in the above described order, and recorded

quantitatively.

In the second group of 50 tracings the same observers were asked to analyze all classifiable variations (type 2 study). Both studies were repeated in a different sequence of the same tracings after three months to determine intra-observer variation. Differences between the type 1 and the type 2 study indicate observer variation caused by omissions of the observers to visually recognize the variations which just met the criteria for a long-term variation and therefore omissions to confirm the amplitude and duration of these variations by using the template.

To investigate the influence of the length of the tracing on the reproducibility of the analysis, each one-hour sample in the type 2 study was divided into consecutive periods of 10 minutes, 20 minutes and 30 minutes, respectively. A comparison was made between the intraobserver variation of the quantity of accelerations in the 50 consecutive periods of 10, 20 and 30 minutes.

STATISTICAL ANALYSIS OF OBSERVER VARIATION.

Agreement between each set of observations (interobserver or intraobserver) was measured by calculating the kappa coefficient, which adjusts for the agreement which can be expected by chance alone[8]. The agreement expected by chance increases with the number of observations in a certain category. Therefore, the kappa coefficient is not necessarily high if most observations lie within one category (e.g. 95% average baseline frequency). A value of +1.00 represents perfect agreement, zero means chance agreement, and negative values represent agreement less than is to be expected on the basis of chance occurrence. Differences between kappa coefficients were tested according to Cohen[8], and because of the high number of comparisons that were made P=0.01 was chosen as the threshold level for statistical significance.

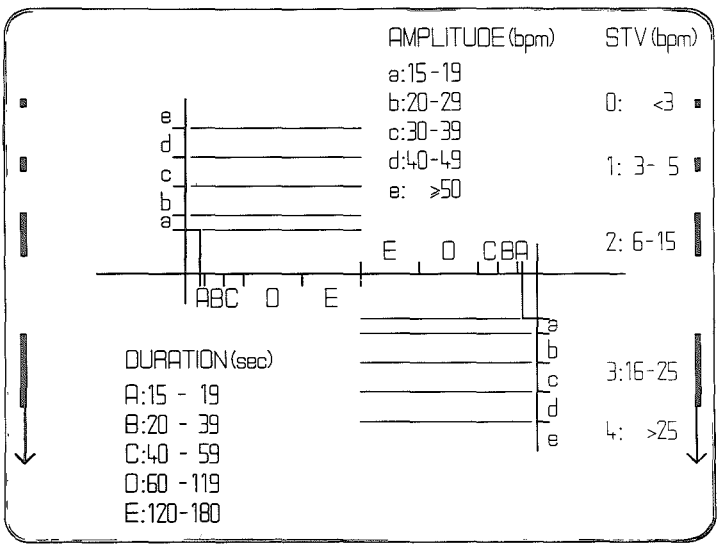

Figure II.2. Transparent template with inscribed classes for the analysis of fetal heart rate patterns.

We also calculated the percentage of almost exact agreement, which includes the disagreement of not more than one value or category.

II.3 R E S U L T S

The 100 hours of tracings contained approximately 650 accelerations and 175 decelerations. In the type 1 study about 350 of the marked heart rate patterns were considered long-term variations. The results of the determination of the intra- and inter-observer variation are shown in table II.2. Acceleration and deceleration durations had the lowest reproducibility, the recognition of the long-term variation types had the highest reproducibility. All kappa coefficients were highly significant ($P<0.001$) when tested against the null hypothesis of no agreement beyond chance. Since the percentages of almost exact agreement are 100 or close to 100, most disagreement concerns differences of not more than one value or class.

Differences between intraobserver variation of both observers and differences between interobserver and intraobserver variation were only once significant ($P<0.01$, table II.2). Only when all long-term varations were assessed (type 2 study) figures for the presence and amount of long-term variations were calculated. No consistent differences in observer variations between both types of study were found.

In the type 2 study 350 long-term variations were recognized by the observers. in 101 of these patterns one of both observers did not consider the pattern a long-term variation, resulting in a classifiability kappa of 0.66. Only 12 of these patterns could not be considered borderline since the observer who considered them long-term variations measured an amplitude of at least 20 bpm or a duration of at least 20 seconds. Therefore, 12 in 700 observed patterns (1.7%) can be considered errors of visual long-term variation recognition.

TABLE II.2. Intraobserver and interobserver variation.[#]

Variable	Intraobserver A		Intraobserver B		Interobserver	
	type 1	type 2	type 1	type 2	type 1	type 2
Baseline frequency	0.83	0.82	0.85	0.91	0.80	0.79
Short-term variability	0.64	0.82	1.00	0.85	0.72	0.79
Long-term variation type	0.99	0.99	0.97	0.97	0.96	0.96
Acceleration shape	0.73	0.82	0.73	0.75	0.71	0.66
	(99)	(99)	(98)	(99)		(99)
Acceleration duration	0.61*	0.78*	0.69	0.76	0.61	0.76
	(97)	(99)	(98)	(98)	(97)	(98)
Acceleration amplitude	0.63*	0.77	0.79*	0.67	0.66	0.74
Acceleration presence		0.77		0.74		0.85
Acceleration amount		0.73		0.77		0.71
Deceleration lagtime	0.81	0.82	0.83	0.79	0.62	0.70
	(94)	(97)	(95)	(95)	(93)	(89)
Deceleration duration	0.73	0.69	0.70	0.62	0.60	0.64
	(89)	(98)			(91)	(96)
Deceleration amplitude	0.77	0.82	0.90*+	0.70*	0.58+	0.67
				(99)	(95)	
Deceleration presence		0.87		0.85		0.91
Deceleration amount		0.93		0.93		0.87
Uterine contractions	0.91	0.78	0.88	0.92	0.73	0.79
		(98)				

#: The observer variation is expressed as kappa coefficients. Differences between observers, between study types and between intra- and inter-observer variations were tested, indicated are $P<0.05$ (* vs *, + vs +). The percentage of almost exact agreement is shown in parentheses (when not shown: 100%).

DURATION OF OBSERVATION.

In the assessment of the number of accelerations per 10 minutes, the agreement between consecutive tracings, measured by kappa coefficients and by the percentages of almost exact agreement, decreased with shorter durations of the tracings (fig. II.3). The kappa coefficients in the 10-and 20-minutes segments were not significantly different from chance agreement.

II.4 C O M M E N T

To allow evaluation of its clinical effectiveness a test must meet two important criteria: 1) the test procedure must be described in sufficient detail to permit exact replication, 2) intra- and inter-observer variation must be known as an indicator of the reproducibility of test results[9].

The only requirement of a system of fetal heart rate monitoring designed to detect fetal distress is, that it allows the obstetrician to distinguish between patterns indicating the presence and patterns indicating the absence of fetal distress, whereas a system designed to study the genesis of various heart rate patterns needs a more detailed classification. Unlike others[1,3] we classified all long-term variations separately, which makes a quantitative analysis possible and can be used in a detailed investigation of the influences of fetal distress and other factors on fetal heart rate variability.

To limit the loss of information to a minimum we used many variables (e.g., the presence or absence of notches in accelerations), in contrast to most computerized systems of analysis, that only use indexes of short-term variability[10,11], of long-term variability[10] or deceleration areas[12].

An important determinant of the reliability of a monitoring system is its reproducibility, which may be enhanced by the use of objective criteria as applied in the classifications presented here. The use of only one criterion to distinguish

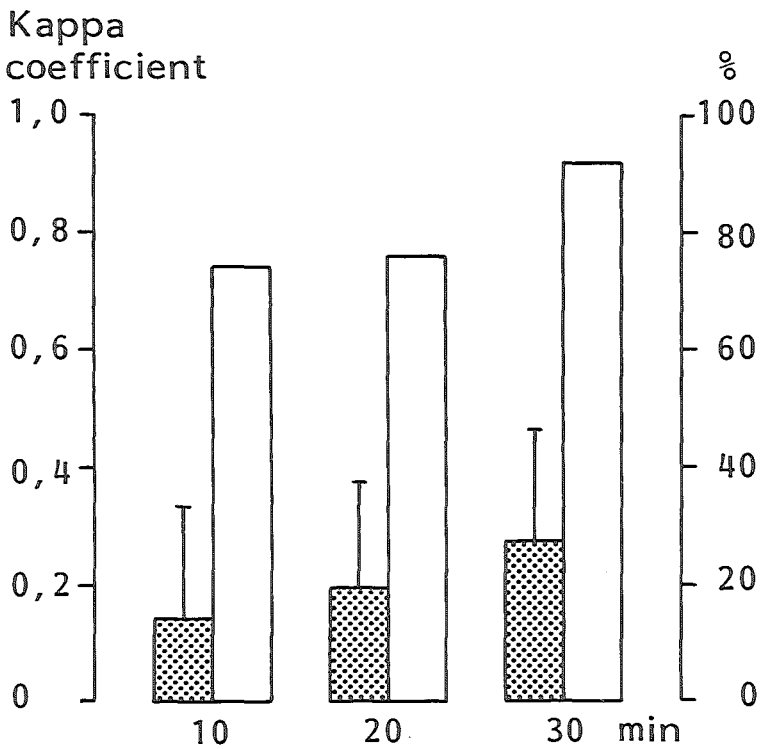

Figure II.3. Agreement with regard to the number of accelerations per 10 minutes between two consecutive tracing segments of 10, 20 and 30 minutes' duration. Shaded bars represent the kappa coefficient (plus two standard deviations), open bars represent the percentage of almost exact agreement.

between classes of heart rate patterns (e.g., the use of lag-time to distinguish between classes of decelerations) prevents the occurrence of unclassifiable patterns and may be expected to increase reproducibility. In the analysis of short-term variability we used the amplitude of short-term variability since determination of the oscillation frequency has been shown to be less reproducible[5].

In contrast to others[4-6] who reported little agreement between observers in the visual assessment of cardiotocographic tracings with or without the use of a scoring system, we showed a high degree of observer agreement for all the variables of the system. The disagreement was mainly based on minor differences.

In contrast to reports in which agreement increased with the experience of the observers[4], the observer with limited experience in this study reached an intraobserver agreement comparable with that of the experienced observer, indicating that experience is not a prerequisite for the reliable application of this system.

The difference between the type 1 and the type 2 study lies in the capability of the observer to decide correctly if an oscillation reaches the minimal duration and amplitude to be considered a long-term variation. Since both types of study showed observer variations of the same order of magnitude, it is concluded that this subjective element in the visual analysis did not influence observer variation.

The comparison between observer variations in consecutive records of 30, 20 and 10 minutes duration showed limited and decreasing agreement, most likely due to biologic variability. This finding indicates that a length of tracing of 60 minutes is preferable.

The classification presented here allows standardized visual analysis and quantification of fetal heart rate patterns with a minimum of observer variability, and will thus make comparisons

possible between studies performed in various centers.

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C H A P T E R III

INTRAPARTUM FETAL HEART RATE PATTERNS II. QUANTIFICATION, TREND DETECTION AND REFERENCE VALUES IN UNCOMPLICATED PREGNANCIES.

III.1 I N T R O D U C T I O N

A quantitative method of analysis of intrapartum fetal heart rate (FHR) patterns was developed, which shows minimal observer variation and a low sensitivity for biologic variability[1]. This method was applied in the present prospective study of FHR patterns obtained during the first stage of labor in women with pregnancies without predefined complications.

The study was designed to determine differences between FHR patterns in the first and in the second half of the first stage (trend detection), to determine the influences of various obstetric factors on FHR patterns, and to establish reference values.

III.2 M A T E R I A L A N D M E T H O D S

For this study 606 caucasian women in labor were selected at the Department of Obstetrics and Gynecology, Ikazia Hospital, Rotterdam, according to the following criteria: one fetus of 37 to 42 weeks gestational age in cephalic position, no previous cesarean section, and no other known factors predisposing to an abnormal mode of delivery. However, women with mild pregnancy-associated hypertension (diastolic blood pressure 90-100 mm Hg, Korotkoff 4) or fetal growth retardation were not excluded. All women had received standard antenatal care in our clinic from the first trimester onwards.

Beginning in the first stage of labor fetal heart rate, derived from the fetal ECG obtained with a scalp electrode, and intrauterine pressure, measured by means of a fluid-filled open-tipped catheter and pressure transducer, were recorded with a Hewlett-Packard monitor type 8030A at a paper speed of one cm per minute. Pethidine-hydrochloride (1 to 2 times 75 mg i.m.) was given for pain relief when necessary and oxytocin by

continuous i.v. was administered for stimulation of hypotonic labor when indicated. The tracings were obtained in various positions, but when the FHR showed decelerations, the left lateral position was preferred. Fetal scalp blood sampling was performed when judged necessary by the attending obstetrician on the basis of a questionable tracing.

There were 330 women with an uncomplicated pregnancy, no pregnancy-associated hypertension, and birth weights above the 10th percentile of the Dutch birth weight tables corrected for parity, gestational age and fetal sex[2]. None of the newborns had congenital malformations. The study group consisted of all 142 of these 330 patients in whom two tracings with a duration of one hour were obtained at the beginning (3-5 cm cervical dilation, phase 1) and the end (7-9 cm cervical dilation, phase 2) of the active phase of labor. These tracings began at least 30 minutes after amniotomy and ended at least 30 minutes before the onset of the second stage. The remaining group of 188 patients, in which the required duration of FHR monitoring was not met, contained more multiparae and more women with a first stage of three hours duration or less than the study group, but there were no interventions because of fetal distress.

ANALYSIS OF THE TRACINGS. Tracings were analyzed quantitatively and qualitatively. The quantitative method of analysis of the FHR with the use of a template and exact criteria, has been described previously[1]. Briefly, each of the FHR patterns was classified according to type, shape, amplitude, duration and relationship to uterine contractions; each class was quantitated in each one-hour tracing. For long-term variations a duration of at least 15 seconds and an amplitude of at least 15 bpm was required. Decelerations were defined as early, intermediate and late according to lag-times of less than 10, of 10-30, and of more than 30 seconds, respectively. In addition to the usual FHR patterns combination-patterns were described, consisting of accelerations joined with

decelerations, as well as accelerations with and without notches of at least 10 bpm. Patterns with a duration of at least 40 seconds and an amplitude of at least 30 bpm were termed "exaggerated". One investigator analyzed the tracings. For the quantitative analysis of accelerations and decelerations, in which the mean value of the FHR pattern concerned was calculated, only tracings showing at least one acceleration or deceleration were used. In this fashion qualitative FHR data could not influence the quantitative FHR analysis.

In the qualitative analysis, the definitions of the FHR patterns were the same as in the quantitative analysis and a one-hour tracing was considered positive for a FHR pattern when it showed at least one such pattern.

STATISTICAL ANALYSIS. Relative frequencies were statistically tested with the Chi-square test, Fisher's exact test, and the McNemar test. Quantitative differences were assessed with the Wilcoxon test for paired or unpaired data. Reference values were defined using the 2.5th and 97.5th percentile of the frequency distribution. Associations between paired FHR data were tested using the kappa coefficient (K)[3] and the Spearman correlation coefficient (R). As the threshold level for statistical significance $p = 0.05$ was chosen. Because of the large number of tests used to assess the relationship between obstetric factors and FHR patterns, $p = 0.025$ was chosen as the threshold level for statistical significance for these tests.

III.3 R E S U L T S

Table III.1 shows pertinent clinical data of the 142 patients. The three cesarean sections were performed for dystocia during the second stage of labor without signs of fetal distress. Seven infants showed a 1-minute Apgar score of 6, two of 5 and one of 4; 7 of these ten neonates had a nuchal cord, an incidence which is significantly higher ($p < 0.01$) than that in the neonates with normal 1-minute Apgar scores. All infants had

TABLE III.1. Clinical data of the study group (n=142).

	No. of women*	
GENERAL DATA		
Age (yrs, median & range)	28	(14 - 47)
Nulliparous	58	
LABOR & PARTURITION		
Meconium-stained amniotic fluid	9	
Pethidine-HCl within 90 min before a tracing	60	
I.v. oxytocin during a tracing	93	
Scalp blood analysis (pH range)	12	(7.28-7.40)
Nuchal cord	40	
Cesarean Section	3	
NEONATAL DATA		
Birth weight (g, median & range)	3390	(2540-4500)
1-minute Apgar score < 7	10	

* unless indicated otherwise.

Apgar scores >7 after 5 minutes.

FETAL HEART RATE PATTERNS.

Qualitative analysis. An absence of long-term variations was observed in 6% of the phase 1 tracings, and in 12% of the phase 2 tracings; the difference is not significant. Phase 2 showed significantly more tracings with accelerations and decelerations occurring in the same recording than phase 1 (32% and 13%, respectively; $p < 0.001$). No significant relationship could be demonstrated between the presence of decelerations in one phase and the presence or absence of accelerations in the other phase. Agreement corrected for chance occurrence with regard to the occurrence of the same FHR patterns in phases 1 and 2 was significant (accelerations: $K = 0.23$, $p < 0.05$, decelerations: $K = 0.18$, $p < 0.05$, accelerations as well as decelerations in the same recording: $K = 0.19$, $p < 0.05$). This indicates an individual consistency in the occurrence of FHR patterns throughout the first stage of labor. The differences between both phases (trend) in the occurrence of most FHR patterns were significant for the whole group of women (Table III.2).

Quantitative analysis. The quantitative data of FHR patterns, the differences between phases 1 and 2, and the associations between FHR patterns in both phases are shown in Table III.2. A baseline frequency below 95 bpm, a short-term variability amplitude below 3 bpm or repetitive late decelerations were never observed. For accelerations the duration of the patterns was significantly associated with the amplitude (phase 1: $R = 0.33$, $p < 0.0001$ and phase 2: $R = 0.44$, $p < 0.0001$). The most frequently occurring acceleration pattern had a duration of 20-40 seconds and an amplitude of 20-30 bpm. In tracings with accelerations mean values of most of the accelerative patterns were lower in phase 2 than in phase 1, whereas tracings with decelerations showed higher mean values of

Table III.2. FHR patterns in phase 1 and 2 of the first stage of labor.

FHR Pattern	Qualitative approach % of patients		Quantitative approach: Mean			Spearman corr.coeff. phase 1-2		2.5-97.5 percentile	
	phase 1	phase 2	phase 1	phase 2				phase 1	phase 2
Baseline frequency (<120 bpm**)	3	4	133	131	#	.69	#	105- 165	105-155
Short-term variab. (≤5 bpm**)	18	31 #	9.2	8.6	+	.50	#	3- 15	3- 25
Accelerations									
during contract.	87	74 *	4.9	4.3		.41	#	0- 14	0- 11
between contract.	56	49 *	2.1	1.1	*	.24	*	0- 8	0- 5
simple shaped	89	72 #	5.0	4.1		.42	#	0- 13	0- 12
notched shaped	54	45	1.9	1.4		.30	#	0- 9	0- 6
non-exaggerated	91	75 #	5.5	4.2	+	.39	#	0- 15	0- 10
exaggerated	43	40	1.4	1.3		.49	#	0- 10	0- 6
total number			6.9	5.5	+	.44	#	0- 18	0- 14
mean amplitude (bpm)			27	29	+	.63	#	0- 38	0- 39
total amplitude (bpm)	91	77 #	197	160		.48	#	0- 580	0-435
mean duration (sec)			45	47		.36	#	0- 95	0- 90
total duration (sec)			324	256		.43	#	0-1088	0-720
Decelerations									
early	9	23 #	1.2	2.1		.25	*	0- 2	0- 7
intermediate	4	12 *	0.5	1.3		.37	#	0- 2	0- 10
late	1	0	0.1	0.0				0- 0	0- 0
combined	3	13 #	0.4	0.4		.17	+	0- 1	0- 2
non-exaggerated	14	38 #	2.0	3.5		.22	*	0- 4	0- 12
exaggerated	3	9	0.2	0.4		.10		0- 1	0- 2
total number	16	41 #	2.2	3.9	+	.24	*	0- 4	0- 14
total number without comb.pat.			2.1	4.2	*	.23	*	0- 3	0- 12
mean amplitude (bpm)	14	34 #	35	34		.23	*	0- 45	0- 55
total amplitude (bpm)			63	131	+	.23	*	0- 100	0-345
mean duration (sec)			40	39		.21	*	0- 50	0- 58
total duration (sec)			76	168	*	.24	*	0- 120	0-390

Statistical significance indicated by + ($p < 0.05$), * ($p < 0.01$) and # ($p < 0.001$). ** indicates the criterion used in the qualitative approach.

most of the decelerative patterns in phase 2. Comparison of the means of the FHR patterns over all tracings revealed that accelerations decreased by 33% (from 6.3 in phase 1 to 4.2 in phase 2, $p < 0.0001$), whereas early, intermediate and combined decelerations increased in phase 2 with a factor 4.4 (0.20 to 0.87, $p = 0.0005$), a factor 7.0 (0.077 to 0.54, $p = 0.004$), and a factor 2.9 (0.063 to 0.18, $p = 0.04$), respectively. For most FHR patterns the Spearman coefficients of correlation between the patterns of phase 1 and phase 2 are highly significant. The number of accelerations shows a significant negative correlation with the number of decelerations (phase 1: $R = -0.20$, $p = 0.008$; phase 2: $R = -0.21$, $p = 0.007$).

Phase 1 and 2 reference values between the 2.5th and 97.5th percentiles are given in Table III.2; values not included in the reference range are defined as abnormal. With regard to an abnormally low short-term variability amplitude or an abnormal baseline frequency or an abnormal number of decelerative patterns, 20 patients (14%, including 2 of the 10 patients with a 1-minute Apgar score below 7) showed an abnormality in at least one of the two one-hour tracings and 11 of these patients (8%) showed at least 2 abnormalities in one hour. Not one of the tracings showed one of the possible combinations of abnormal baseline frequency, abnormally low short-term variability amplitude or an abnormal number of decelerative patterns. An abnormal number of accelerative patterns never appeared in combination with an abnormal number of decelerative patterns or an abnormally low short-term variability amplitude. Baseline frequencies below 120 or above 160 bpm in one or both phases were observed in 4% of the women, a short-term variability amplitude of 5 bpm or lower in 35%, and two or more variable (exaggerated) decelerations or late decelerations in 4%; these "classic" cutoff values of abnormality resulted in much higher percentages of patients with abnormal tracings.

The significant associations between FHR patterns and obstetric

factors are shown in Table III.3. Parity, the presence or absence of meconium-stained amniotic fluid, mode of delivery, and birth weight did not show a significant relationship with any of the FHR patterns. Some of the obstetric factors or changes in these factors during the first stage were significantly related to observed differences (trend) in the number of long- term variations or in the values for the short-term variability or baseline frequency, between phase 1 and phase 2 (Table III.4).

III.3 C O M M E N T

As judged by neonatal outcome it seems unlikely that any of the fetuses suffered significant distress during the first stage of labor. For that reason this study allows determination of reference values for physiologic intrapartum FHR patterns. Tracings of one hour duration were used, because a previous study showed a low reproducibility for tracings of 30 minutes' duration or less[1].

The absence of a significant relationship between FHR accelerations and decelerations in the same, the previous, or the subsequent recording, does not support observations reported by others indicating that the presence of accelerations increases the chance of subsequent occurrence of decelerations[4]. In the present study group of uncomplicated labors exaggerated accelerations were frequently observed. The occurrence of such accelerations was significantly related to a high 1-minute Apgar score, which supports earlier reports that the occurrence of exaggerated accelerations is reassuring[5].

A relationship between FHR patterns and 1-minute Apgar score was only found in phase 2. In phase 2 accelerations between contractions were not observed in tracings of women who were delivered of an infant with a 1-minute Apgar score below 7. It has been reported[6,7] that there is no relationship between Apgar scores and FHR patterns early in the first stage of labor. This

Table III.3. Relationship between obstetric factors and FHR patterns in the first stage of labor; only significant relations ($p < 0.025$) are shown.

Obstetric Factor	Fetal Heart Rate Pattern	Phase	Mean value of FHR pattern when obstetric factor		
			Present	Absent	
Duration of gestation ≤39 weeks.	Baseline frequency (bpm)	1	136	132	+
	Decel. exaggerated	2	0.9	0.2	+
Oxytocin stimulation during the tracing.	Accel. between contractions	1	1.3	2.6	*
	Accel. non-exaggerated	1	4.6	6.2	+
Pethidine-HCl within 90 min before the beginning of the tracing.	Baseline frequency (bpm)	1	128	134	+
	Accel. during contractions	2	3.4	4.9	#
	Accel. simple shaped	2	2.9	4.9	#
	Accel. non-exaggerated	2	3.2	4.9	*
	Accel. total number	2	4.1	6.4	*
	Accel. total amplitude (bpm)	2	124	183	*
	Accel. total duration (sec)	2	195	296	+
Uterine contractions >20 per hour.	Accel. between contractions	1	1.2	2.8	#
Second stage of >30 min duration.	Decel. early	1	4.0	0.6	*
Nuchal cord.	Decel. intermediate	2	2.3	0.6	+
	Decel. presence (% of cases)	2	63	32	*
Sex of fetus (female).	Baseline frequency (bpm)	1	136	131	*
	Short-term variability (bpm)	1	9	10	+
	Baseline frequency (bpm)	2	133	129	*
Apgar score < 7 after one min.	Accel. between contractions	2	0.0	1.2	*
	Accel. exaggerated	2	0.1	1.4	+

+ $p < 0.025$, * $p < 0.01$ and # $p < 0.001$.

Table III.4. Relationship between obstetric factors and the difference (trend) in FHR patterns between phase 1 and 2; only significant ($p < 0.025$) relations are shown.

Obstetric Factor	Fetal Heart Rate Pattern	Mean increase (+) or decrease (-) of FHR pattern in phase 2 if obstetric factor is		
		present	absent	
Pethidine-HCl only in phase 2.	Short-term variability (bpm)	-2.1	-0.1	#
	Accel. total number	-3.7	-1.5	*
Oxytocin only in phase 2.	Accel. between contractions	-2.3	-0.6	**
Uterine contr. > 20/hour only in phase 2.	Accel. between contractions	-1.6	-0.7	*
Nuchal cord.	Decel. intermediate	+1.3	+0.1	**
	Decel. non-exaggerated	+2.2	+0.7	*
	Decel. total number	+2.6	+0.7	*

* $p < 0.025$, ** $p < 0.01$ and # $p < 0.001$.

may be caused by the association between a variety of obstetric factors and FHR patterns as demonstrated in this study. For instance, in phase 1 administration of pethidine-hydrochloride was found to be related to a fall in baseline frequency, and oxytocine stimulation to a decrease in two types of accelerations. Significant relationships between obstetric factors and FHR patterns were mainly observed when the FHR patterns were analyzed quantitatively, indicating the relevance of quantitation.

For almost all FHR patterns significant tendency to differ in occurrence between phase 1 and 2 was demonstrated. Some of these trends, like those concerning the total number of accelerations and the total number of decelerations have been described in high-risk patients[8]. The present data do not support the suggestion that these trends may be useful to predict neonatal outcome[9]. A relationship between a trend in any of the FHR patterns and the Apgar score could not be shown. However, some of the observed trends could be explained in part by the following obstetric factors: a high uterine contraction frequency, a nuchal cord, and oxytocin- and pethidine-administration.

It has been shown that pethidine reduces long-term and short-term variability between uterine contractions[10]. This finding is supported by the present data, indicating that in presumably healthy fetuses pethidine causes a fall in the number of non-exaggerated and simple accelerations, and in the number of accelerations during contractions, as well as in baseline frequency and short-term variability amplitude.

The described trends make it necessary to use separate reference values for the first and the second half of the first stage. The reference values as determined in our study indicate that the absence of accelerations, moderate bradycardia (105-120 bpm), moderate short-term variability amplitude (3-6 bpm) and to some extent even variable and exaggerated decelerations may be

considered part of a physiologic pattern of FHR variations. This is in agreement with results of other studies which indicate that moderate fetal bradycardia during labor is not necessarily indicative of fetal distress[11].

The use of reference values as established in the present study may help to reduce the high incidence of false positive test results as reported in the literature[12].

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CHAPTER IV

INTRAPARTUM FETAL HEART RATE PATTERNS III. OBSERVER VARIABILITY IN THE ANALYSIS AND INTERPRETATION OF FHR TRACINGS

IV.1 I N T R O D U C T I O N

The considerable observer variability that occurs in the analysis as well as in the clinical interpretation of FHR patterns constitutes an important limitation of antepartum and intrapartum FHR monitoring[1-6].

The observer variability is limited for each of the FHR variables analyzed separately. However, the variables are considered together in the analysis of one-hour tracings. The aim of this study is to determine the magnitude of the observer variability in the assessment of one-hour FHR tracings with the use of quantitated reference values.

IV.2 M A T E R I A L A N D M E T H O D S

QUANTITATIVE ANALYSIS OF FHR PATTERNS.

Fifty tracings were selected from 200 one-hour FHR tracings obtained at 3-5 cm cervical dilation (phase 1 of the first stage of labor) in 200 consecutive term patients regarded as being "high risk". Selection was performed in such a way, that the tracings contained a wide range of baseline frequencies, short- and long-term variations. All FHR patterns were analyzed and quantitated twice with a 3 months'interval by an experienced obstetrician and a resident in obstetrics with limited experience, with the use of a standardized method, objective criteria and a transparent template. The method and results of these analyses were shown in chapter II of this thesis.

INTERPRETATION OF THE ANALYSIS.

From the 50 tracings data were obtained concerning 50 baseline frequencies, 50 short-term variabilities and approximately 475 long-term variations. The first set of analyses by both

observers was used for clinical interpretation of FHR patterns. The tracings were labeled normal or abnormal on the basis the quantitated reference values for baseline frequency, short-term variability amplitude and for the frequencies of occurrence of the various decelerations. These reference values were described in chapter III of this thesis for phase 1 (3-5 cm cervical dilation) of the first stage of labor, and are summarized in Table IV.1. A tracing was interpreted as "abnormal" if one or more values of the quantitated FHR patterns were outside the reference range. After three months the procedure was repeated to obtain a second set of analyses and interpretations of the same tracings.

STATISTICAL ANALYSIS OF OBSERVER VARIABILITY.

Agreement between each set of interpretations (intraobserver or interobserver) was assessed by calculating the kappa coefficient, which adjusts for agreement to be expected by chance alone[7]. The agreement by chance increases with the number of observations in a certain category. Therefore, the kappa coefficient is not necessarily high if most observations lie within one category (e.g. 95% normal tracings) A value of +1.00 represents perfect agreement, zero indicates chance agreement, and negative values represent agreement less than is to be expected on the basis of chance occurrence.

IV.3 R E S U L T S

As shown in Table IV.2 the percentage of agreement in all four interpretations was 86%. Disagreement concerned tracings which were considered normal on the basis of one interpretation only, as well as tracings which were labeled abnormal on the basis of one interpretation only.

Intraobserver agreement was 90% and 92%, resulting in kappa coefficients of 0.85 and 0.83, respectively. Interobserver

Table IV.1. Reference values for phase 1 (3-5 cm cervical dilation) of the first stage of labor.

FHR Pattern	Reference Value Range
Baseline frequency (bpm)	105 - 165
Short-term variability amplitude (bpm)	3 - 15
Decelerations (numbers per hour)	
early	0 - 2
intermediate	0 - 2
late	0 - 0
combined	0 - 1
non-exaggerated	0 - 4
exaggerated	0 - 1
total number	0 - 4

Table IV.2. Resuls of four interpretations of 50 FHR tracings, by two observers.

number of normal interpretations	number of FHR tracings (%)
all 4	25 (50)
only 3	4 (8)
only 2	1 (2)
only 1	2 (4)
none	18 (36)

agreement was 92% and 92%, resulting in kappa coefficients of 0.84. All these kappa coefficients are significantly above chance agreement ($p < 0.00001$).

IV.4 C O M M E N T

The two observers, who differed in experience, showed almost the same intraobserver variability. A lack of any effect of experience on interobserver variability was shown before in antepartum FHR monitoring[3].

The magnitudes of intra- and interobserver variability of the interpretation of complete one-hour FHR tracings are similar to the results of the observer agreement on each FHR variation separately, as described in chapter II of this thesis. It should be noted that with an observer disagreement of approximately 16% (corrected for chance agreement) a sensitivity and specificity of a test in the order of magnitude of 100% cannot be possible. Indices of FHR variability derived by computer[8,9] have the advantage of absence of observer variation in the analysis of the FHR variations. However, in the interpretation of a tracing these computer methods make use of only few of the many different FHR patterns or they use normal values which are not based on clinical studies.

The in this thesis described method of standardization of detailed observation of FHR tracings with the use of objective criteria and a template, and of interpretation using clinically determined quantitated reference values results in an observer variability that is low compared to that obtained in other studies[1-6]. For that reason the application of this method appears to be attractive, in particular when results obtained in different groups of patients and in different centers are to be compared.

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CHAPTER V

INTRAPARTUM FETAL HEART RATE PATTERNS IV. QUANTIFICATION AND TREND DETECTION IN SMALL-FOR-GESTATIONAL AGE FETUSES

V.1 I N T R O D U C T I O N

The value of fetal heart rate (FHR) monitoring should be assessed in each group of women considered to be at risk[1]. Women with small-for-gestational age (SGA) fetuses are at risk for the development of intrapartum fetal distress[2]. Preterm SGA fetuses as well as the much larger group of term SGA fetuses show an increased risk for the development of cerebral palsy[3]. The fetal weight-gestational age percentile can be used as an indicator of risk for chronic fetal distress. Various reports show conflicting results concerning the relationship between qualitatively assessed FHR patterns and the fetal weight-gestational age percentile in preterm- and term SGA fetuses[2,4,5]. Qualitative assessment of patterns in FHR tracings is associated with a relatively high rate of false positive and false negative tests[6], and with a low observer agreement[7].

In the present study a previously described method of quantitative assessment of FHR patterns with a low observer variation[8,9] was applied, to compare intrapartum FHR patterns of term SGA fetuses obtained during the first stage of labor with those of appropriate-for-gestational age (AGA) term fetuses. The second aim of the study was to assess the value of previous determined reference values[8] in predicting fetal distress in term SGA fetuses.

V.2 M A T E R I A L A N D M E T H O D S

This study was part of a larger prospective study comprising 606 caucasean women in labor at the Department of Obstetrics and Gynecology of the Ikazia Hospital, Rotterdam[8]. In all cases there was a single fetus in cephalic position with a gestational age of 37 to 42 weeks, no previous cesarean section, and no

other known factors predisposing to an abnormal mode of delivery. However, women with suspected fetal growth retardation or mild pregnancy-associated hypertension (diastolic blood pressure 90-100 mm Hg, Korotkoff phase 4) were not excluded. All women had received standard antenatal care from the first trimester onwards.

Beginning in the first stage of labor, fetal heart rate, derived from the fetal ECG obtained with a scalp electrode, and intrauterine pressure, measured by means of a fluid-filled open-tipped catheter and pressure transducer, were recorded with a Hewlett-Packard monitor type 8030A at a paper speed of one cm per minute. Pethidine-hydrochloride (i.m. 1 to 2 times 75 mg) was given for pain relief when necessary and oxytocine by continuous i.v. was administered for stimulation of hypotonic labor, when indicated. The tracings were obtained in various positions, but when the FHR showed decelerations, the left lateral position was preferred. Fetal scalp blood sampling was performed when judged necessary by the attending obstetrician on the basis of a questionable tracing.

Of the 606 women 130 were delivered of a fetus with a weight below the 10th percentile of the Dutch birthweight tables corrected for parity, gestational age and fetal sex[10]. None of the newborns had congenital malformations. The study group consisted of all 70 of these 130 patients in whom two tracings with a duration of one hour were obtained at the beginning (3-5 cm cervical dilation, phase 1) and the end (7-9cm cervical dilation, phase 2) of the first stage of labor. These tracings began at least 30 minutes after amniotomy and ended at least 30 minutes before the onset of the second stage. The remaining 60 patients, in which the required duration of FHR monitoring was not met, showed six intrapartum cesarean sections for fetal distress, but all infants survived and did well.

Data from 142 of the 606 women who had had uncomplicated pregnancies and were delivered of term AGA fetuses were reported previously[8], and were used as controls in this study.

ANALYSIS OF THE TRACINGS. Tracings were analyzed qualitatively and quantitatively. The quantitative method of analysis of FHR tracings used in this study was described previously[9]. Briefly, each of the FHR patterns was classified according to type, shape, amplitude, duration and relationship to uterine contractions; each class was quantitated in each one-hour tracing. For long-term variations a duration of at least 15 seconds and an amplitude of at least 15 bpm was required. Decelerations were defined as early, intermediate and late according to lag-times of less than 10, of 10-30, and of more than 30 seconds, respectively. In addition to the usual FHR patterns combination patterns were described, consisting of accelerations joined with decelerations, as well as accelerations with and without notches of at least 10 bpm. Patterns with a duration of at least 40 seconds and an amplitude of at least 30 bpm were termed "exaggerated". One investigator analyzed the tracings. For the quantitative analysis of accelerations and decelerations, in which the mean value of the FHR pattern concerned was calculated, only tracings that showed at least one acceleration or deceleration were used in the assessment of the relationship between FHR patterns and various obstetric factors other than fetal distress. In this fashion qualitative FHR data could not influence the quantitative FHR analysis. In the qualitative analysis, the definitions of the FHR patterns were the same as in the quantitative analysis and a one-hour tracing was considered positive for a FHR pattern when it showed at least one such pattern.

STATISTICAL ANALYSIS. Relative frequencies were statistically tested with the Chi-square test, Fisher's exact test and the

McNemar test. Quantitative differences were assessed with the Wilcoxon test for paired or unpaired data. Reference values were defined using the 2.5th and 97.5th percentile of the frequency distribution. The Spearman correlation coefficient was used as a measure of association between quantitative FHR variables. As the threshold level for statistical significance $p = 0.05$ was chosen. Because of the large number of tests used to assess the relationship between obstetric factors and FHR patterns, $p = 0.025$ was chosen as the threshold level for statistical significance, for these tests.

V.3 R E S U L T S

Table V.1 shows pertinent clinical data of the 70 patients. Parity, the frequency of oxytocin-, and pethidine administration, and the incidence of a nuchal cord did not differ significantly between the 70 women with SGA infants and the 142 AGA controls.

Fetal distress, defined as a 1-minute Apgar score <7 and/or a scalp blood pH <7.25, was present in 15 SGA fetuses, and in 10 AGA fetuses ($p < 0.05$). Fetal distress was significantly correlated with the presence of meconium-stained amniotic fluid ($p < 0.01$) and with vacuum-extraction ($p < 0.01$), and it was not associated with pethidine- or oxytocin administration, a nuchal cord, or parity. All infants did well, one newborn had a 5-minute Apgar score <7.

FETAL HEART RATE PATTERNS. Table V.2 shows the results of the FHR analysis. Differences in FHR patterns between SGA and AGA fetuses were more pronounced in phase 1 than in phase 2; in phase 1 SGA fetuses showed significantly more late decelerations, and less accelerations. These differences could also be demonstrated within separate groups of fetuses with and without distress. In SGA fetuses, differences between FHR patterns in phases 1 and 2 were significant only for some of the

TABLE V.1. Clinical data of the study group and the control group.

	study group* (n=70)		control group* (n=142)	
GENERAL DATA				
Age (yrs, median & range)	29	(16-43)	28	(14-47)
Nulliparous	35		58	
Pregnancy-associated hypertension	18		0#	
LABOR & PARTURITION				
Meconium-stained amniotic fluid	5		9	
Pethidine-HCl within 90 min before a tracing	30		60	
I.v. oxytocin during a tracing	42		93	
Scalp blood sampling	22		12#	
of which pH <7.25	8		0#	
Nuchal cord	27		40	
Cesarean section	1		3	
NEONATAL				
1-minute Apgar score <7	12		10#	
Birth weight (g, median & range)	2570	(1350-2995)	3390#	(2540-4500)
Birth weight < P 5	30		0#	
Birth weight < P 2.5	13		0#	

* Number of patients, unless indicated otherwise.

# $p < 0.05$ (control versus study group).

Table V.2. FHR data obtained in the study group and in the control group.

FHR Pattern	Study group n=70				Control group n=142	
	%		mean value		mean value	
	phase 1	phase 2	phase 1	phase 2	phase 1	phase 2
Baseline frequency (<120 bpm**)	1	1	135	134	133	131 #*
Short-term variability (≤5 bpm**)	33	40	8.3	7.7	9.2*	8.6#
Accelerations during contr.	70	59	3.1	3.5	4.4*	3.3#
between contr.	37	29	1.2	0.7	1.9*	0.9#
simple-shaped	70	54#	3.4	3.0	4.6*	3.2#
notched-shaped	36	50	0.9	1.2	1.7*	1.0#
non-exaggerated	73	56#	3.5	3.5	5.0*	3.2#
exaggerated	29	30	0.8	0.7	1.3	1.0
total number			4.3	4.2	6.3*	4.2#
mean amplitude (bpm)			20	16 #	25 *	22 *
total amplitude(bpm)	73	59#	122	118	179 *	123 #
mean duration (sec)			35	30	41	36
total duration (sec)			211	216	295 *	197 #
Decelerations early	6	20#	0.3	1.2#	0.2	0.9#
intermediate	20	23	0.6	2.0#	0.1*	0.5#*
late	10	11	0.5	0.4	0.0*	0.0 *
combined	10	11	0.2	0.2	0.1*	0.2#
non-exaggerated	29	43#	1.1	2.6#	0.3*	1.4#
exaggerated	16	24	0.5	1.3	0.0*	0.2#*
total number	31	47#	1.6	3.9#	0.4*	1.6#
total minus combined			1.4	3.7#	0.3*	1.4#*
mean amplitude (bpm)			10	18 #	5 *	11 #*
total amplitude(bpm)	29	44#	49	146 #	9 *	44 #*
mean duration (sec)			15	19	6 *	13 #
total duration (sec)			92	174 #	11 *	57 #*

* $p < 0.05$, control vs study cases; # $p < 0.05$, phase 1 vs 2.

** Criterion used in the qualitative analysis.

long-term variations; the differences were of a smaller magnitude than those in AGA controls. The profile of FHR patterns in phase 1 of the SGA group resembled that observed in phase 2 of the AGA group. The correlation between FHR patterns in phase 1 and in phase 2 indicates to what extent fetuses with a high frequency of occurrence of some FHR pattern in phase 1, show that pattern also in phase 2. Spearman correlation coefficients were lowest for combined decelerations ($R = 0.20$, $p = 0.05$), and highest for late decelerations ($R = 0.94$, $p < 0.001$). In AGA controls Spearman coefficients ranged from 0.10 to 0.69, and were significant for all FHR patterns except the relatively infrequently occurring late and exaggerated decelerations.

Various quantitated variables concerning long-term variations showed a significant relationship ($p < 0.025$) with the following obstetric factors: a gestational age of <40 weeks, nulliparity, pregnancy-associated hypertension, meconium-stained amniotic fluid, pethidine- and oxytocin administration, uterine contractions >20/hour, 1-minute Apgar score <7, and a birth weight <P2.3. Short-term variability amplitude was significantly lower in case of pethidine administration or pregnancy-associated hypertension. Baseline frequency was not correlated with any of the obstetric factors mentioned. The only factor that showed no significant relationship to FHR was a nuchal cord. Of the qualitatively analyzed FHR patterns decelerations occurred significantly more frequently in case of pethidine administration, a 1-minute Apgar score <7, or a birth weight <P2.3.

Of the absolute values and of the differences between values in both phases (trends) of all FHR patterns shown in Table V.2, only the values of various quantitatively assessed long-term variations were related ($p < 0.01$) to the occurrence of fetal distress (Table V.3).

Table V.3. Relationships between FHR patterns and fetal distress (1-min. Apgar score <7 or scalp blood pH <7.25).

FHR pattern	Mean value of FHR pattern			
	Phase 1, distress		Phase 2, distress	
	-	+	-	+
Accelerations				
during contraction			4.1	1.3
simple-shaped	3.9	1.3	3.6	0.8
total number			4.9	1.7
mean amplitude (bpm)			18.5	7.0
total amplitude(bpm)			137.0	48.7
mean duration (sec)			34.1	12.6
total duration (sec)			251.0	83.7
Decelerations				
late	0.02	2.3	0.04	1.9
non-exaggerated	0.5	3.3	2.0	4.8
exaggerated	0.1	2.0	0.8	3.1
total number	0.6	5.3	2.8	7.9
total minus combined	0.4	5.1	2.5	7.9
mean amplitude (bpm)	6.8	22.9		
total amplitude(bpm)	18.1	164.3	101.5	310.2
mean duration (sec)	6.8	44.0	14.6	36.4
total duration (sec)	17.9	364.2	108.5	411.5

Reference values for baseline frequency, short-term variability and frequencies of occurrence of the various decelerations were used to predict fetal distress in phase 1 and 2 (Table V.4). In the study group all predictive indices are somewhat higher in phase 1 than in phase 2. Defining a test positive in phase 2 only if the test in phase 1 was also positive gave the best predictive indices in both groups. None of the 6 study fetuses who had a FHR out of the reference range in phase 2 only, showed signs of distress. Therefore, considering a test in phase 2 positive if FHR patterns in phase 1 or in phase 2 show a value outside the reference range did not improve the prediction of fetal distress. The addition of FHR data and reference values concerning means and totals of amplitudes and durations of decelerations did also not improve the prediction.

Instead of quantitative reference values, we also applied "classic" cutoff values (a baseline frequency below 120 or above 160 bpm, a short-term variability amplitude of 5 bpm or lower, or repetitive late or exaggerated-variable decelerations). Defining a test positive if in phase 1 and in phase 2 one of the FHR patterns showed a value beyond these "classic" cutoff values gave a sensitivity in the study group of only 33%, and a specificity of 75%. In neither phase the use of "classic" cutoff values showed a significantly ($p>0.05$) higher relative frequency of distressed fetuses in the group with a positive test than in the group with a negative test.

Of the 13 study cases with FHR patterns outside the reference range in both phases and a 1-minute Apgar score <7, 3 cases (23%) had a scalp pH >7.25, indicating that in cases with persistent FHR values outside the reference range a single non-acidotic scalp blood sample is insufficient to predict an Apgar score >7.

V.4 C O M M E N T

Intrapartum distress as defined by a 1-minute Apgar score <7

Table V.4. Prediction of a 1-minute Apgar score <7 and/or a scalp blood pH <7.25 with the use of quantitated FHR Patterns. All data are percentages.

	Study group (n = 70) First stage of labor			Control group (n = 142) First stage of labor		
	Phase 1	Phase 2	Phase 1+2	Phase 1	Phase 2	Phase 1+2
Positive tests*						
True	16	13	13	0	1	0
False	7	14	6	8	5	1
Predictive value	69#	47#	70#	8	22	50
Negative tests						
True	71	64	72	86	88	93
False	6	9	9	6	6	6
Predictive value	93	88	89	93	94	94
Sensitivity	73	60	60	10	22	10
Specificity	91	82	93	92	95	99

* A test is positive if one of the FHR patterns showed a value out of the reference range in one of the phases or in phase 1 as well as in phase 2 ('phase 1+2').

The relative frequency of distressed fetuses is significantly higher in the group with a positive test than in the group with a negative test ($p < 0.05$).

and/or a scalp blood pH <7.25 was observed significantly more often in SGA than in AGA fetuses, but it was mild in most cases. In our group of women differences between Apgar scores of SGA and AGA infants were found to be related to fetal growth retardation and associated factors only, not to factors such as administration of pethidine or oxytocin, or a nuchal cord.

Several publications indicate an association of low fetal weight relative to gestational age with increased occurrence of early[4], variable[4,5], and late[2,4] decelerations during a period of time of a few hours prior to delivery. The present study generally supports these findings; in SGA fetuses as compared to AGA controls we showed a decreased short-term variability amplitude, in particular in phase 1, decreased numbers of various accelerations and increased numbers of all decelerations (except early decelerations), as well as an increased baseline frequency in phase 2.

In the present study associations between FHR patterns and obstetric factors in SGA fetuses are generally comparable to those observed in AGA fetuses[8]. However, in the SGA but not in the AGA group pethidine administration was associated with an increase in the number of decelerations, and a nuchal cord was not associated with any of the FHR patterns. Assessing these associations it should be realized that the obstetric factors investigated are not independent.

It has been suggested that abnormal FHR patterns may be related to a factor other than fetal distress[11] associated with growth retardation, since in SGA fetuses no relationship was found between acid-base status during elective cesarean sections and antepartum FHR patterns, although the latter differed from FHR patterns in AGA fetuses. The present data support this suggestion: significant differences in FHR patterns between AGA and SGA fetuses, with or without fetal distress were observed; these differences were most striking in phase 1. A brain-

sparing effect on blood flow distribution as described in normally grown fetal lambs during acute reduction of the arterial oxygen content[12] and in the human growth-retarded fetus[13], may explain the absence of a relationship between FHR patterns and a nuchal cord. A decreased ratio of umbilical to cerebral blood flow may cause a decreased influence of umbilical compression on the blood pressure and baroreceptors within the carotid artery, and therefore a decreased influence on FHR.

In SGA fetuses the sensitivity of prediction of fetal distress from FHR patterns was higher and specificity was somewhat lower than in the AGA fetuses. Predictive values of positive or negative tests are dependent on the prevalence of fetal distress. Thus, studies on the prediction of fetal distress are only comparable if the populations from which patients are drawn are comparable. Therefore, the same population of SGA fetuses was used to compare the use of "classic" cutoff values with the use of quantitated reference values; with the latter an early prediction of fetal distress was possible.

In the literature the use of total durations of FHR patterns rather than total numbers to predict fetal distress has been described before. In nonstress testing the total acceleration duration may be useful in assessing fetal condition[14]. Such a relationship could not be shown in our study. The present intrapartum data also show that the prediction of fetal distress was not improved by adding data of means and totals of amplitudes and durations of decelerations. In SGA and in AGA[8] fetuses the number of notched accelerations was not significantly related to the occurrence of distress.

It has been suggested that trend analysis of intrapartum FHR data may be useful to predict fetal condition[15]. However, the present data indicate that in AGA[8] and in SGA fetuses the differences in numbers of FHR patterns between both phases (trends, including the trend in total acceleration duration) were not associated with fetal distress.

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CHAPTER VI

INTRAPARTUM FETAL HEART RATE PATTERNS V. QUANTIFICATION AND TREND DETECTION IN COMPLICATED PREGNANCIES

VI.1 I N T R O D U C T I O N

In the present prospective study of fetal heart rate (FHR) patterns during the first stage of labor a recently developed method of quantitative assessment with a low observer variation[1] was applied. This method was used previously in a study of intrapartum FHR patterns in women with uncomplicated pregnancies[2] and in women with pregnancies complicated by fetal growth retardation terminating in the delivery of small-for-gestational age (SGA) infants[3]. It has been proposed that the value of FHR monitoring should be assessed separately in each group of women considered to be at risk[4].

For this reason the present study was designed to compare FHR patterns obtained during the first stage of labor in patients with hypertension, postmaturity, or another pregnancy complication, with FHR patterns in appropriate-for-gestational age (AGA) controls with uncomplicated pregnancies. The second aim was to assess the value of previously determined reference values[2] in predicting fetal distress.

VI.2 M A T E R I A L A N D M E T H O D S

This study was part of a larger prospective study of caucasean women in labor at the Department of Obstetrics and Gynecology of the Ikazia Hospital, Rotterdam[2,3]. In all cases there was a single fetus in cephalic position, a gestation of 37 to 42 weeks, no previous cesarean section or repeat instrumental delivery. The total study group (n=902) was divided in the following subgroups: uncomplicated pregnancies (n=330), women who were delivered of an SGA infant (n=130), and pregnancies with complications other than fetal growth retardation (n=442).

Results obtained in women with uncomplicated pregnancies and in patients who were delivered of SGA infants were described previously[2,3]; this report concerns the last subgroup of 442 women with complicated pregnancies, who were delivered of a fetus with a birth weight above the 10th percentile, according to the Dutch birth weight tables corrected for parity, gestational age and fetal sex[5]. All women received standard antenatal care from the first trimester onwards.

Beginning in the first stage of labor FHR, derived from the fetal ECG obtained with a scalp electrode, and intrauterine pressure, measured by means of a fluid-filled open-tipped catheter and pressure transducer, were recorded with a Hewlett-Packard monitor type 8030A at a paper speed of one cm per minute. Pethidine-hydrochloride (1 to 2 times 75 mg i.m.) only was given for pain relief when necessary, and oxytocine was administered by continuous intravenous infusion for stimulation of hypotonic labor, when indicated. The tracings were obtained in various positions, but when the FHR showed decelerations, the left lateral position was preferred. Fetal scalp blood sampling was performed when judged necessary by the attending obstetrician on the basis of a questionable tracing.

The final study group consisted of 202 of 442 patients in whom two tracings with a duration of one hour were obtained at 3-5 cm and 7-9 cm cervical dilation (phase 1 and phase 2 of the first stage of labor), respectively. These tracings began at least 30 minutes after amniotomy and ended at least 30 minutes before the onset of the second stage. In the remaining 240 patients, in whom two one-hour tracings were not available, six intrapartum cesareans sections were done for fetal distress, but all infants survived and did well. These cesarean sections were done in women with postmaturity (4), with mild pregnancy-associated hypertension (1), and with a rupture of the membranes for more than 24 hour before the start of active labor (1).

Data from 142 patients, with uncomplicated pregnancies who were delivered of term AGA fetuses were used as controls[2].

ANALYSIS OF THE TRACINGS. In the quantitative method of analysis of the FHR, each of the FHR patterns was classified according to type, shape, amplitude, duration and relationship to uterine contractions; each class was quantitated in each one-hour tracing[1]. For long-term variations a duration of at least 15 seconds and an amplitude of at least 15 bpm was required. Decelerations were defined as early, intermediate and late according to lag-times of less than 10, of 10-30, and of more than 30 seconds, respectively. In addition to the usual FHR patterns combination patterns were described, consisting of accelerations joined with decelerations, as well as accelerations with and without notches of at least 10 bpm. Patterns with a duration of at least 40 seconds and an amplitude of at least 30 bpm were termed "exaggerated". One investigator analyzed the tracings.

STATISTICAL ANALYSIS. Relative frequencies were statistically tested with the Chi-square test, Fisher's exact test and the McNemar test. Quantitative differences were assessed with the Wilcoxon test for paired or unpaired data. A p-value of <0.05 was considered to represent statistical significance. To define abnormal values for baseline frequency, short-term variability and frequencies of occurrence of the various decelerations, the 2.5th and 97.5th percentile of the frequency distribution determined in a previous study of reference values, were used[2]. In the qualitative interpretation of the FHR tracings , a tracing was considered positive when it showed one or more FHR patterns out of the reference range.

V.3 R E S U L T S

Table VI.1 shows the pertinent clinical data of the 202 patients. The group designated as "other complications"

TABLE VI.1. Clinical data.

DATA		hypertensive pregnancies n=86	postdate pregnancies n=39	other complications n=77	controls (uncomplicated) n=142
GENERAL					
Age	median	27	26*	26*	28
	range	19-46	19-35	18-47	14-47
Nulliparous	%	66*	77*	66*	41
LABOR & PARTURITION					
Gestational	median	39*	42*	40	40
age (weeks)	range	37-41	42-44	37-41	37-41
Meconium-stained amniotic fluid	%	1	13	22**	6
Pethidine-HCl#	%	38	51	43	42
I.v. oxytocin during a tracing	%	59	49	68	65
Scalp blood analysis	%	15	23*	26*	8
pH < 7.25	n	4*	1	0	0
Nuchal cord	%	38	33	32	28
NEONATAL					
1-min Apgar score <7	%	15*	10	6	7
Birth weight	median	3090*	3630*	3330	3390
	range	2275-4710	2790-5000	2350-5060	2540-4500

* Significantly different from the control patients ($p < 0.05$).

** This group included the 11 women with meconium-stained amniotic fluid as the only pregnancy complication.

Within 90 min before a tracing.

consisted of women with ruptured membranes for more than 24 hours before the beginning of active labor (24), women with meconium stained amniotic fluid as the only observed complication before active labor (11), vaginal hemorrhage before active labor (9), abnormal glucose tolerance test (5), arrest of spontaneous labor before 4 cm cervical dilation (9), and various other complications (19). Of the 86 women with mild pregnancy-associated hypertension (diastolic blood pressure 90-100 mm Hg, Korotkoff phase 4) 16 (19%) had a fetus with a scalp pH < 7.25 and/or were delivered of an infant with a 1-minute Apgar score <7, which is a significantly higher number ($p<0.01$) than in the control group. For postdate women and for the group "other complications" these figures were 13% and 6%, respectively. The infants of hypertensive patients had significantly ($p<0.05$) lower birth weights than those of control women. There was one intrapartum cesarean section in the study group, in a postdate woman because of fetal distress (scalp blood pH 7.05).

In Table VI.2 the results of the quantitative FHR analysis are shown. Only 8 late decelerations were observed in the 688 hours of registration. Table VI.3 presents predictive indices of fetal distress as defined by a 1-minute Apgar score <7 and/or a scalp blood pH <7.25. The use of "classic" cutoff values (a baseline frequency below 120 or above 160 bpm, a short-term variability amplitude of 5 bpm or lower, or repetive late or exaggerated-variable decelerations) showed relatively low predictive indices, which were not improved by the use of reference values. With the use of the latter, the number of false positive tests was lower than with the use of the classic cutoff values in all groups with pregnancy complications, as well as in the control group.

VI.4 C O M M E N T

The data shows significant differences between phase 1 and 2

Table VI.2. FHR Data, mean values.

FHR Pattern	Control women n = 142 phase		Hypertensives n = 86 phase		Post dates n = 39 phase		Others n = 77 phase	
	1	2	1	2	1	2	1	2
Baseline frequency (bpm)	133	131#	132	129#	129*	129	132	129#
Short-term variab. (bpm)	9.2	8.6#	8.0*	7.6	9.2	8.3	8.7	8.7
Accelerations								
during contr.	4.4	3.3#	3.6	2.6#	4.0	2.6#	4.3	3.6
between contr.	1.9	0.9#	1.2*	0.6#	1.1	0.3*#	0.9*	0.5#
simple-shaped	4.6	3.2#	3.5*	2.5#	4.2	2.4#	4.2	3.2#
notched-shaped	1.7	1.0#	1.3	0.7*#	0.9	0.6	1.0	0.9
non-exaggerated	5.0	3.2#	3.7*	2.7#	4.0	2.4#	4.3	3.4
exaggerated	1.3	1.0	1.0	0.5*	1.1	0.6	1.0	0.7
total number	6.3	4.2#	4.8*	3.2*#	5.1	2.9	5.2	4.1
Decelerations								
early	0.2	0.9#	0.1	1.5#	0.3	1.1#	0.3	0.8#
intermediate	0.1	0.5#	0.1	0.7#	0.0	0.2	0.0	0.1
late	0.0	0.0	0.0	0.0	0.1	0.1	0.0	0.0
combined	0.1	0.2#	0.1	0.2	0.0	0.1	0.0	0.2#
non-exaggerated	0.3	1.4#	0.2	2.2#	0.3	1.3#	0.3	0.9#
exaggerated	0.0	0.2#	0.1	0.3	0.1	0.2	0.1	0.1
total number	0.4	1.6#	0.3	2.5#	0.4	1.5#	0.3	1.0#
total minus combined	0.3	1.4#	0.2	2.2#	0.4	1.4#	0.3	0.9#

* $p < 0.05$, control vs study cases; # $p < 0.05$, phase 1 vs 2.

Table VI.3. Prediction of a 1-minute Apgar score < 7 and/or a scalp blood pH < 7.25, with the use of FHR Patterns.

Phase of first stage	FHR inter-pretation	correctly predicted %	false positives %	predictive value of a positive test %	predictive value of a negative test %	sensi-tivity %	speci-ficity %
Controls (n=142)							
Phase 1+2	ref. values	93	1	50	94	10	99
Phase 1+2	classic	82	13	17	95	40	86
Hypertensives (n=86)							
Phase 1+2	ref. values	80	3	25	82	6	96
Phase 1+2	classic	67	24	28	58	50	71
Post-dates (n=39)							
Phase 1+2	ref. values	85	3	0	87	0	97
Phase 1+2	classic	74	15	14	88	25	82
Others (n=77)							
Phase 1+2	ref. values	91	3	1	93	0	97
Phase 1+2	classic	81	13	0	93	0	86

* A test is considered positive if at least one FHR patterns showed a value out of the reference range.

with regard to many quantitatively assessed FHR patterns. Such differences were also demonstrated in uncomplicated pregnancies[2], and in pregnancies complicated by an SGA fetus[3]. These findings implicate that the phase of the first stage of labor should be taken into account in the assessment of FHR tracings.

A relatively low baseline frequency was observed in postdate fetuses. A progressive decrease in FHR baseline frequency from 19 to 40 weeks gestation has been demonstrated in antepartum FHR tracings, and is considered a result of maturation of the autonomic nervous system[6]. The finding of significantly lower values of short-term variability and of various accelerative FHR patterns in hypertensive women as compared to controls is at variance with the results of another study[7], in which differences in occurrence of FHR patterns were attributed to magnesium sulfate medication only. The findings in the present study cannot be attributed to sedative or antihypertensive medication, which was not used in any of the patients.

In each group of pregnancy complications the occurrence of accelerations between contractions was the only FHR pattern that showed significantly lower values than in the control group. This was previously observed also in SGA fetuses[3]. In uncomplicated pregnancies this FHR pattern was one of the few patterns significantly associated with a 1-minute Apgar score >7[2]; therefore, this pattern may be the most sensitive indicator of the absence of (mild) fetal distress.

With the use of predefined reference values as well as with "classic" cut-off values rather poor predictive indices of fetal distress were obtained. This is in contrast to data obtained in SGA fetuses, in which the use of reference values allowed good prediction[3]. Fetal distress observed in the present study was mild, and probably not of a chronic character as may have been the case in SGA fetuses. Low Apgar scores may have been caused

by events occurring after 9 cm cervical dilation, thus not affecting the earlier obtained FHR tracings. This is in accordance with the finding that in the present study low Apgar scores were usually not associated with a low scalp pH, as observed in SGA fetuses[3]. This explanation of the low predictive power of intrapartum FHR patterns in low risk women is supported by the absent or very limited benefit of FHR monitoring demonstrated in two recently conducted prospective trials[8,9]. Since a recent report indicated that fetal scalp blood sampling is rarely used in clinical practice[10], the number of false positive test results is important in the cost/benefit analysis of FHR monitoring. The use of reference values as described in this study will increase the detection of early intrapartum fetal distress as occurring in SGA fetuses[3], and at the same time it may be expected to reduce the rate of false positive tests which is responsible for a low benefit/cost ratio in low risk patients.

VI.5 R E F E R E N C E S

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SUMMARY AND CONCLUSIONS

In CHAPTER I the history and present status of fetal heart rate (FHR) monitoring are outlined. Various problems are associated with the early prediction of fetal distress, whether auscultation or electronic FHR monitoring (EFM) is used. This may be the cause of the disappointing results of eight prospective clinical trials comparing EFM with auscultation. The problems concern the reliability of analysis of FHR tracings in terms of method and detail of classification of FHR patterns, observer variation in the analysis of FHR patterns, as well as the reliability of the interpretation of the results of the analysis in terms of definition of normal values, and of observer variation. Studies in which it is attempted to investigate these problems, and possible improvements, need a design which allows the assessment of observer variation of a standardized quantitative analysis of FHR patterns with the use of a systematic and detailed classification, the influence of biologic variability on that analysis, the determination of reference values, the estimation of the relative importance of the different FHR patterns, and assessment of the reliability of the early prediction of fetal distress.

In CHAPTER II the detailed classification of the FHR patterns as used throughout this thesis is described. This classification consists of different sets of criteria that are applicable to each FHR pattern, exactly defined, mutually exclusive, and complementary. In appendix one the classification of FHR patterns is further demonstrated with the use of a number of figures. The standardized method of quantitative analysis of baseline frequency, short-term and long-term variability, with the use of a template and based on tracings with a duration of one hour is also described. The

intraobserver and the interobserver variations were determined by calculating kappa coefficients. These ranged from 0.58 (interobserver deceleration amplitude) to 0.99 (intraobserver long-term variation type), indicating close agreement within and between observers. It is further concluded that the duration of tracings to be analyzed quantitatively should be longer than 30 minutes. The latter criterion is based on the results of a study of the biologic variability of the occurrence of FHR patterns in consecutive FHR tracings.

In CHAPTER III the study is described of FHR patterns during the first stage of labor in 142 women with uncomplicated pregnancies and an appropriate-for-gestational age infant. A significant difference (trend) in the occurrence and frequency of FHR patterns between phase 1 (3-5 cm cervical dilation) and phase 2 (7-9 cm cervical dilation) was demonstrated. As compared with the first phase, the second phase showed a significant decrease in the mean values of baseline frequency, short-term variability, and the occurrence of accelerations. The frequency of occurrence of early, variable, and combined decelerations increased significantly in the second phase. It is demonstrated that various obstetric factors are related to the occurrence and frequency of FHR patterns. Qualitative analysis of FHR patterns revealed lèss of the above described differences and relationships than quantitative analysis. The occurrence of exaggerated FHR accelerations or of FHR accelerations between uterine contractions was significantly associated with a 1-minute Apgar score >6. The occurrence of FHR accelerations did not precede the occurrence of FHR decelerations later in the first stage of labor. The differences in FHR patterns between both phases made it necessary that separate reference values for both phases were calculated from the FHR data. These reference values showed

that the absence of FHR accelerations, moderate bradycardia, moderate short-term variability amplitude, and to some extent even variable and exaggerated FHR decelerations, may be considered part of a physiologic pattern of FHR variations.

In CHAPTER IV it is shown that the interpretation of the tracings analyzed in chapter two with the use of the reference values as described in chapter three resulted in a low intra- and inter-observer variability. Kappa coefficients determined to assess intra- and inter-observer variability ranged from 0.83 to 0.85. It is concluded that the limited observer variation in the analysis of each separate FHR pattern did not result in a large observer variation in the interpretation of a complete one-hour tracing. Therefore, the detailed classification of FHR patterns, the standardized method of quantitative analysis, and the interpretation of this analysis with the use of reference values can be used for the comparison of different groups of patients or of results of different centers.

In CHAPTER V the results are described of the quantitative analysis of intrapartum FHR patterns in 70 women with a small-for-gestational age (SGA) infant and no other complications than mild pregnancy-associated hypertenson. A significant difference in the occurrence of FHR patterns was shown between appropriate-for-gestational age (AGA) and SGA fetuses, with or without fetal distress. Within the group of SGA fetuses a significant difference (trend) in the occurrence of FHR patterns was shown between phase 1 and phase 2 of the first stage of labor. The profile of patterns in phase 1 of the SGA group was almost similar to that in phase 2 of the AGA group. Significant relationships between these trends and the occurrence of fetal distress could not be demonstrated, neither in AGA, nor in SGA fetuses.

Various FHR patterns were significantly related to obstetric factors. In phase 1 predefined reference values for the patterns showed a sensitivity of 73%, and a specificity of 91% in predicting the 21% of infants with a 1-minute Apgar score <7 and/or a scalp blood pH<7.25. The prediction of fetal distress showed a higher predictive power with the use of the reference values than with the use of the "classic" cut-off values.

In CHAPTER VI the results are shown obtained in 202 women with various pregnancy complications other than a small-for-gestational age infant. Comparison of the FHR patterns of phase 2 with those of phase 1 showed a decrease in some accelerations and an increase in decelerations in phase 2. These trends were comparable to those observed in 142 control women with uncomplicated pregnancies. As compared to control women significantly lower values were found in hypertensive women for short-term variability and various accelerative FHR patterns, in postdate women for baseline frequency and accelerations between contractions, and in the group of women with other complications for accelerations between contractions. Differences in occurrence of patterns and in prediction of fetal distress were not consistent between the various types of pregnancy complications. The use of quantitated reference values did not improve the low power of the prediction of fetal distress as shown with the use of "classic" cutoff values, although it reduced the rate of false positive tests by a factor 8.

GENERAL CONCLUSION.

Various changes in the technique of analysis and interpretation of FHR tracings as described in this thesis improve the early prediction of the presence or absence of fetal distress. The improvement is due to a reduced observer variation in the

analysis and in the interpretation of FHR tracings as well as to an improved validity of the assessment.

The use of a qualitative analysis of FHR patterns and of "classic" cut-off values in the interpretation of FHR tracings must be considered of limited value in the early prediction of fetal distress. The use of a quantitative analysis of FHR patterns and of quantitated reference values for interpretation of FHR tracings improves the early prediction of fetal distress by reducing the number of false negative tests in small-for-gestational age fetuses, and by reducing the number of false positive tests in all groups of pregnancy complications studied.

A reliable technique of FHR assessment is a prerequisite not only for the clinical application of electronic fetal monitoring, but also for the comparison of different groups of patients or of results obtained in different centers. These issues may be considered to be of importance in the design of prospective clinical trials with the aim to assess the cost/benefit ratio of electronic fetal monitoring.

SAMENVATTING EN CONCLUSIES.

In HOOFDSTUK I wordt de geschiedenis geschetst van de bewaking van de foetale hartslagfrequentie (cardiotocografie) en wordt de tegenwoordige stand van zaken uiteengezet. Met de vroege voorspelling van foetale nood hangt een aantal problemen samen, ongeacht of auscultatie dan wel cardiotocografie wordt gebruikt. Dit zou de oorzaak kunnen zijn van de teleurstellende resultaten verkregen in acht prospectieve klinische onderzoekingen waarin cardiotocografie wordt vergeleken met auscultatie. De genoemde problemen betreffen de betrouwbaarheid van de analyse van cardiotocogrammen voor wat betreft de methodiek en de gedetailleerdheid van de classificatie van foetale hartslag frequentie (FHF) patronen, alsmede de betrouwbaarheid van de interpretatie van de resultaten van de analyse voor wat betreft de definiëring van normaal-waarden en de variatie binnen en tussen observatoren. Onderzoekingen waarin wordt getracht deze problemen en de mogelijke oplossingen ervan te onderzoeken, moeten op zodanige wijze zijn opgezet, dat de observator-variatie van een gedetailleerde kwantitatieve analyse van FHF patronen, met gebruikmaking van een systematische en gedetailleerde classificatie, kan worden beoordeeld. Ook moet het mogelijk zijn om de invloed van de biologische variatie op de analyse te beoordelen, referentie waarden te bepalen, het relatieve gewicht van de verschillende FHF patronen te schatten en de betrouwbaarheid te beoordelen van de vroege voorspelling van foetale nood.

In HOOFDSTUK II wordt de gedetailleerde classificatie beschreven van FHF patronen die wordt gebruikt in dit proefschrift. Deze classificatie bestaat uit verschillende groepen criteria, die op elk FHF patroon kunnen worden

toegepast, die exact zijn gedefinieerd, en die elkaar uitsluiten en complementair zijn. In Appendix 1 wordt de classificatie van FHF patronen nader gedemonstreerd met gebruik van een aantal figuren. De gestandaardiseerde methode van kwantitatieve analyse van basishartfrequentie, short- en long-term variaties met gebruik van een sjabloon en gebaseerd op een duur van de registraties van één uur, wordt beschreven. De variaties binnen en tussen observatoren werden bepaald door Kappa coëfficienten te berekenen. Deze varieerden van 0.58 (variatie in deceleratie-amplitudo tussen observatoren) tot 0.99 (variatie in long-term FHF variatie-type binnen observatoren); dit wijst op grote overeenkomst binnen en tussen observatoren. Er wordt verder geconcludeerd dat de duur van de registraties voor een kwantitatieve analyse langer dan 30 minuten moet bedragen. Dit criterium wordt gebaseerd op de resultaten van een onderzoek van de biologische variatie in het voorkomen van FHF patronen in opeenvolgende cardiotocogrammen.

In HOOFDSTUK III wordt het onderzoek beschreven van FHF patronen gedurende de ontsluitingsfase van de baring bij 142 vrouwen met ongecompliceerd verlopen zwangerschappen en met neonatale geboortegewichten passend bij de zwangerschapsduur (appropriate-for-gestational age, AGA). Er was een significant verschil (trend) aantoonbaar tussen de 1e fase (3-5 cm cervicale ontsluiting) en de 2e fase (7-9 cm cervicale ontsluiting), zowel in het voorkomen als in de frequentie van FHF patronen. Vergeleken met de 1e fase toonde de 2e fase een significante afname van de gemiddelde waarden van de basishartfrequentie, de short-term variabiliteit, en het voorkomen van accelerations. De frequentie van voorkomen van vroege, variabele en gecombineerde decelerations nam in de 2e fase significant toe. Er wordt aangetoond dat verschillende obstetrische factoren zijn gerelateerd aan het voorkomen en de frequentie van bepaalde FHF

patronen. Bij kwalitatieve analyse van FHF patronen bleken er minder van de bovenbeschreven verschillen en relaties te kunnen worden aangetoond dan bij kwantitatieve analyse. Het voorkomen van grote FHF accelerations of van accelerations tussen de weeën bleek significant te zijn geassocieerd met een Apgar score >6 na één minuut. Het voorkomen van FHF accelerations bleek geen voorbode te zijn van het optreden van FHF decelerations later in de ontsluitingsfase. De verschillen in FHF patronen tussen de 1e en 2e fase maakte het noodzakelijk om afzonderlijke referentie-waarden te berekenen voor beide fases. Met behulp van deze referentie-waarden werd aangetoond dat afwezigheid van FHF accelerations, een lichte bradycardie (105-120 bpm), een short-term variatie amplitudo van slechts 3-6 bpm en zelfs variabele en grote decelerations kunnen worden beschouwd als een onderdeel van het fysiologisch patroon van FHF variaties.

In HOOFDSTUK IV wordt beschreven dat de interpretatie van de in hoofdstuk II geanalyseerde registraties met gebruik van de in hoofdstuk III beschreven referentie-waarden leidt tot een geringe variatie binnen en tussen observatoren, met Kappa coëfficienten van 0.83 tot 0.85. De beperkte observator variatie in de analyse van elk FHF patroon apart bleek niet te leiden tot een grote observator-variatie in de interpretatie van complete registraties van één uur. Daarom kan de gedetailleerde classificatie van FHF patronen, met een gestandaardiseerde methode van kwantitatieve analyse en de interpretatie van deze analyse met gebruik van referentie-waarden, worden toegepast ter vergelijking van verschillende groepen patienten of van de resultaten verkregen in verschillende centra.

In HOOFDSTUK V worden de resultaten beschreven van de kwantitatieve analyse van FHF patronen tijdens de baring bij 70 vrouwen die een kind kregen met een geboortegewicht lager dan

passend bij de zwangerschapsduur (small-for-gestational age, SGA) en geen andere complicaties dan milde, met de zwangerschap geassocieerde, hypertensie. Er werd een significant verschil aangetoond in het voorkomen van bepaalde FHF patronen tussen AGA en SGA foetus, ongeacht de aanwezigheid van foetale nood. Binnen de groep SGA foetus werd een significant verschil aangetoond (trend) tussen de 1e en 2e fase van de ontsluitingsfase voor wat betreft het voorkomen van bepaalde FHF patronen. Het profiel van de patronen in fase 1 in de SGA groep was bijna gelijk aan dat in de 2e fase in de AGA groep. Significante verbanden tussen deze trends en het voorkomen van foetale nood konden niet worden aangetoond, niet in de AGA groep en ook niet in de SGA groep. Voor verschillende FHF patronen werden significante relaties aangetoond met obstetrische factoren. Met betrekking tot het voorspellen van de 21% van de kinderen met een Apgar score na één minuut <7 en/of een schedel bloed pH<7.25 gaven de vooraf gedefinieerde referentie-waarden voor FHF patronen in de 1e fase een sensitiviteit van 73% en een specificiteit van 91%. De toepassing van referentie-waarden liet een duidelijk betere voorspeling toe van foetale nood dan gebruik van de "klassieke" normen.

In HOOFDSTUK VI worden de resultaten getoond verkregen bij 202 vrouwen met verschillende zwangerschapscomplicaties anders dan een SGA pasgeborene. Vergelijking van de FHF patronen in de 1e fase met die in de 2e fase toonde een afname van een aantal vormen van accelerаties en een toename van de decelerаties in de 2e fase. Deze trends waren vergelijkbaar met die bij 142 controle zwangeren met ongecompliceerde zwangerschappen. In vergelijking met controle zwangeren werden bij vrouwen met hypertensie significant lagere waarden gevonden voor wat betreft short-term variabiliteit en verschillende acceleratieve FHF patronen. Bij serotiene zwangeren werden lagere waarden gevonden

voor de basishartfrequentie en voor accelleraties tussen de weeën en in de groep vrouwen met "overige complicaties" voor acceleraties tussen de weeën. De verschillen in voorkomen van FHF patronen en in voorspelling van foetale nood tussen de groepen met verschillende complicaties van de zwangerschap waren niet consistent. De toepassing van gekwantificeerde referentie-waarden bleek het geringe vermogen van de "klassieke" normen om foetale nood te voorspellen niet te verbeteren, maar het reduceerde wel het aantal vals-positieve testen met een factor 8.

ALGEMENE CONCLUSIE

Verschillende veranderingen in de methoden van analyse en interpretatie van cardiotocogrammen, zoals beschreven in dit proefschrift, verbeteren de vroege voorspelling van de aan- of afwezigheid van foetale nood. Deze verbetering is het gevolg van een verminderde observator-variatie bij de analyse en interpretatie van FHF registraties, alsmede van een verbeterde validiteit van de beoordeling.

De waarde voor vroege voorspelling van foetale nood van het gebruik van een kwalitatieve analyse van FHF patronen en van "klassieke" normen bij de beoordeling van cardiotocogrammen is beperkt. De toepassing van een kwantitatieve analyse en van kwantitatieve referentie waarden bij de interpretatie van cardiotocogrammen verbetert de vroege voorspelling van foetale nood door vermindering van het aantal fout-negatieve testen bij SGA foetus en door vermindering van het aantal fout-positieve testen bij alle overige bestudeerde groepen ongeborenen.

Een betrouwbare methode voor beoordeling van cardiotocogrammen is een voorwaarde, niet alleen voor de klinische toepassing van de cardiotocografie, maar ook voor vergelijking van verschillende groepen patienten en van resultaten verkregen in verschillende centra. Dit alles kan van belang worden beschouwd

bij het ontwerpen van prospectieve klinische onderzoeken met als doel de kosten/baten verhouding van de cardiotocografie te bepalen.

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APPENDIX 1.

In this appendix some aspects of the FHR classification described in this thesis are outlined by figures, for the sake of illustration and reproducibility.

BASELINE FREQUENCY:

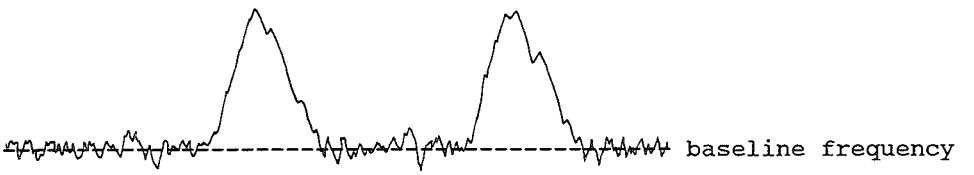

Figure 1. Baseline frequency interference by long-term and short-term variations. The baseline frequency is defined as the mean of all short-term variations occurring in the absence of long-term variations.

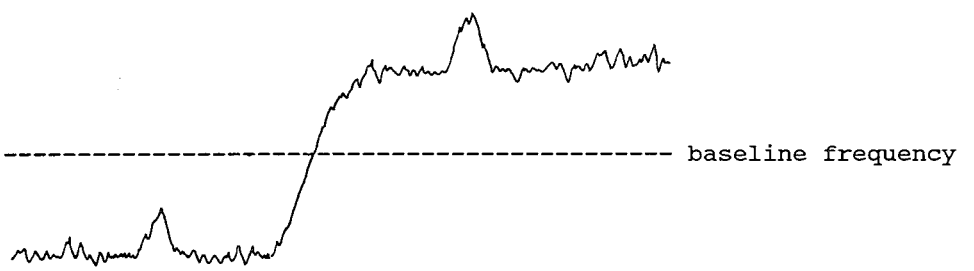

Figure 2. Baseline alterations during a one-hour tracing. The baseline is defined as the mean of all alterations in the baseline frequency.

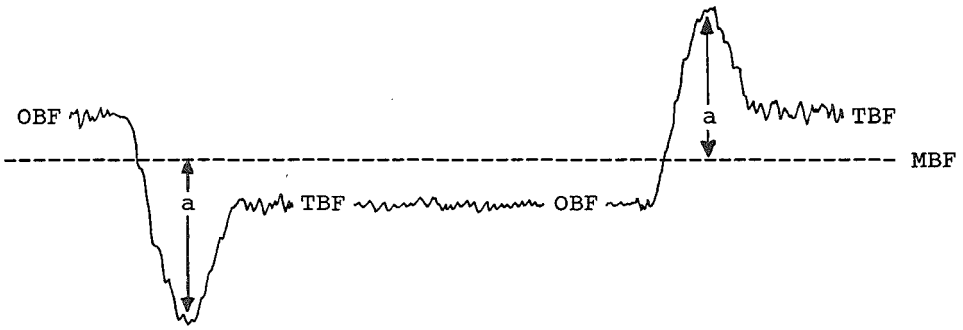

Figure 3. Baseline frequency and the amplitude of long-term variations. A temporary mean baseline frequency (MBF) was introduced for the determination of the amplitude (a) of a long-term variation. MBF is defined as the mean of baseline frequencies before the onset (OBF) and after the termination of the long-term variation (TBF). MBF may deviate from the baseline frequency of the complete one-hour tracing.

LONG-TERM VARIATIONS:

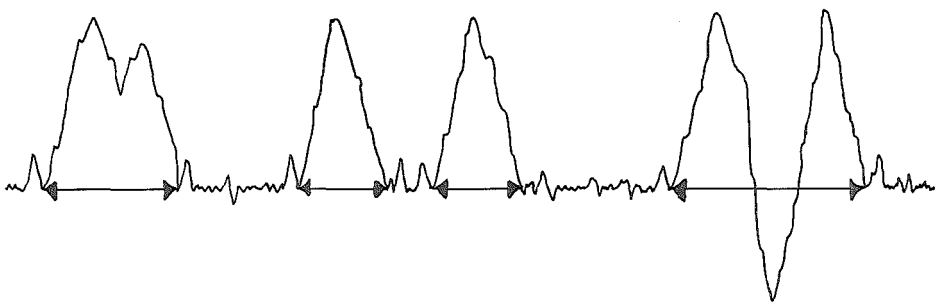

Figure 4. Long-term variation composed of more than one component. Only succesive parts with each an amplitude of at least 15 beats per minute and a duration of at least 15 second contribute to a composed long-term variation, which may consist of accelerating and decelerating parts (combined patterns).

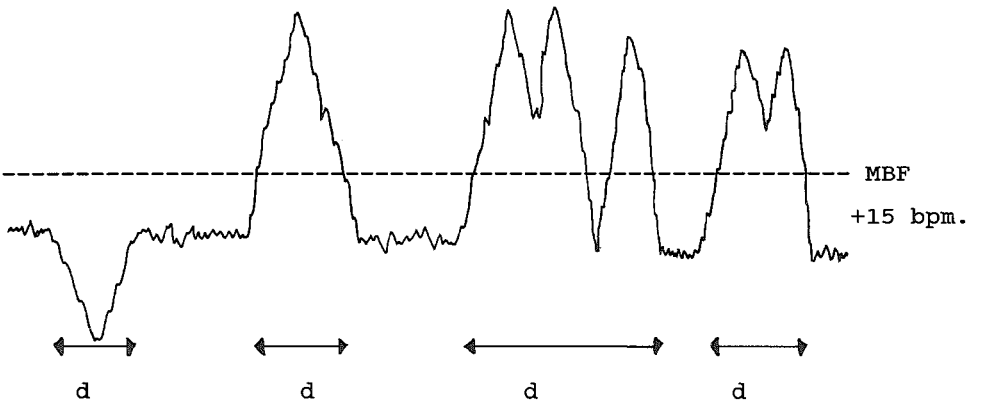

Figure 5. Long-term variations and superimposed short-term variations. Superimposed variations with an amplitude less than 10 beats per minute are neglected and cause decelerations or simple shaped accelerations, larger variations superimposed on accelerations will cause M- or N-notched accelerations. In the determination of the duration (d) of a long-term variation oscillations with an amplitude of more than 10 bpm which do not deviate at least 15 bpm from the MBF during at least 15 seconds, are not considered part of that long-term variation.

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