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**ST analysis of the fetal ECG
as an adjunct to
fetal heart rate monitoring
in labour – a clinical validation**

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Abstract

ST analysis of the fetal ECG as an adjunct to FHR monitoring in labour – a clinical validation.

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The ability to make an accurate assessment of fetal well-being during labour is a great challenge. Animal and human studies have shown that fetal hypoxemia during labour can alter the shape of the fetal electrocardiogram (FECG) waveform, notable elevation of the T-wave and depression of the ST segment. A new medical device (STAN, Neoventa Medical, Mölndal, Sweden) has been developed to monitor the FECG during labour as an adjunct to continuous electronic FHR monitoring (CTG+ST analysis). Before a more general clinical use the technique has been the object of three randomised trials. The present thesis concerns the implementation of this new technique into clinical practice.

At Sahlgrenska hospital, Göteborg, Sweden, 4830 out of 14687 (32.9%) term deliveries were monitored between October 2000 and September 2002. While the number of monitored cases increased from 28.1% in the first year to 37.7% during the second year, the frequency of metabolic acidosis (pH <7.05 and $BD_{\text{cef}} > 12 \text{ mmol/l}$) decreased from 0.76% to 0.44% in all patients and from 1.12% to 0.56% in the CTG+ST monitored group assessed to be in need of close surveillance. The number of operative deliveries was unaltered (**Paper I**).

In a retrospective study at Varberg district hospital labour ward, covering the total population of deliveries during 2004 and 2005, 59% of the deliveries (1875/3193) were monitored with CTG+ST. The metabolic acidosis rate was 0.5%. Crash Caesarean sections (CS) were significantly reduced from 1.5% in the conventionally monitored (CTG) group to 0.3% in the CTG+ST group (**Paper II**). It was concluded that the frequency of metabolic acidosis in this large number of deliveries from Göteborg and Varberg is the same as noted in the CTG+ST group in a Swedish randomised trial on CTG+ST analysis.

Cases originating from a European Union commission supported multi-centre study where CTG+ST had been used together with fetal blood sampling (FBS) were analysed. Of the 911 cases, 53 had cord artery pH <7.06 and 44 had cord artery pH 7.06 -7.09. These cases were analysed together with 97 control cases. CTG+ST clinical guidelines identified all adequately monitored cases with metabolic acidosis requiring special neonatal care. These cases were identified at least 19 minutes prior to delivery. In 22 cases, FBS was obtained 13 (7-24) minutes after CTG+ST guidelines had indicated abnormality and in eight no ST changes had occurred at time of FBS. The corresponding FBS data were pH 7.10 (7.01 – 7.15) and pH 7.21 (7.08 – 7.31), respectively, $p=0.01$. In cases of metabolic acidosis, scalp-pH fell 0.01 units per minute after a ST change rise had been recorded during second stage of labour. In 43 out of 53 cases with cord artery pH <7.06 CTG + ST indicated intervention. In five cases no ST data existed and in the rest of the cases there were no ST indications. One of these newborn had metabolic acidosis but was clinically unaffected (**Paper III and IV**).

The time factor, i.e. the time between onset of significant ST events and delivery can be illustrated by the observation that of those with CTG+ST events recorded within 16 minutes of delivery, 61% had cord artery pH ≥ 7.20 . The corresponding figure for cases where CTG+ST indications occurred more than 16 minutes before delivery was 19% (OR 6.66, 2.29 – 19.86, $p<0.001$).

In conclusion, these data indicate that ST analysis of the FECG identifies a term fetus exposed to hypoxia during labour in a reliable way. FBS has a role in fetal monitoring, e.g. when a CTG+ST recording starts late in labour with abnormal CTG.

Keywords: fetal ECG, ST analysis, electronic fetal monitoring, cardiotocography, fetal blood sampling, metabolic acidosis.

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List of original papers

The thesis is based on the following papers, which are referred to in the text by their roman numerals I-IV

- I. **STAN in clinical practice – The outcome of 2 years of regular use in the city of Gothenburg.**
Håkan Norén, Sofia Blad, Ann Carlsson, Anders Flisberg, Annika Gustavsson, Håkan Lilja, Margareta Wennergren, Henrik Hagberg. Am J Obstet Gynecol 2006;195:7-15.
- II. **STAN, a clinical audit: the outcome of 2 years of regular use in the city of Varberg, Sweden.**
Anna-Karin Welin, Håkan Norén, Anders Odeback, Mona Andersson, Gunnel Andersson, KG Rosén. Acta Obstet Gynecol Scand 2007;86: 827-32.
- III. **Fetal scalp pH and ST analysis of the fetal ECG as an adjunct to CTG. A multi-center, observational study.**
Andreas Luttkus, Håkan Norén, Jens Stupin, Sofia Blad, Sabaratnam Arulkumaran, Rista Erkkola, Henrik Hagberg, Carsten Lenstrup, Gerard Visser, Onning Tamazian, Branka Yli, Karl Rosén, Joachim Dudenhausen. J. Perinat. Med 2004;32:486-94.
- IV. **Fetal scalp pH and ST analysis of the fetal ECG as an adjunct to cardiotocography to predict fetal acidosis in labor.**
Håkan Norén, Andreas Luttkus, Jens Stupin, Sofia Blad, Sabaratnam Arulkumaran, Risto Erkkola, Roberto Luzietti, Gerard Visser, Branka Yli, Karl Rosén. 2007;35:408-14.

Abbreviations

AS	Apgar score
BD _{ecf}	base deficit
BE	base excess
CTG	cardiotocography
CoE	centre of excellence
CO ₂	carbon dioxide
CP	cerebral palsy
CNS	central nervous system
ECG	electrocardiogram
ECF	extracellular fluid
EFM	electronic fetal monitoring
FECG	fetal electrocardiogram
FBS	fetal blood sampling
FIGO	International federation of Gynaecologists and Obstetricians
FTP	failure to progress
GOT	Göteborg
H ⁺	hydrogen
HCO ₃	hydrogen carbonate
H ₂ CO ₃	carbonic acid
H ₂ O	water
HIE	hypoxic ischemic encephalopathy
IUGR	intrauterine growth retardation
K ⁺	potassium ion
NICU	neonatal intensive care unit
ODFD	operative delivery for fetal distress
OR	odds ratio
pO ₂	partial pressure of oxygen
pCO ₂	partial pressure of carbon dioxide
RCT	randomised controlled trial
SCBU	special care baby unit
SD	standard deviation
ST	ST segment of the electrocardiogram
STAN	fetal monitor with ST analysis
SVD	spontaneous vaginal delivery
VE	vacuum extraction
QI	quality improvement

Introduction

Fetal monitoring during labour constitutes a challenge in information management. Until today labour staff has managed this complex situation by visual analysis of a host of information. Recent developments have identified the possibility of not only adding new information from ST waveform analysis of the fetal electrocardiogram (FECG) but also applying computer assisted ST data interpretation thereby reducing ambiguity and improving coherence with clinical guidelines.

Adverse events in early life are known to have an impact on both child development and long-term adult health. Perinatal brain injury in particular constitutes a major clinical hazard. Hypoxic-ischemic brain injury as a result of oxygen deficiency (asphyxia) during labour at term continues to be a problem. Ambiguity in interpreting CTG patterns is one factor behind 'defensive medicine' and increasing operative intervention rates. Clearly, this is not a situation that will satisfy anyone and we should consider what measures can be taken to improve perinatal outcome. Such an analysis would include the application of physiological models to enhance the interpretation of the FECG during delivery.

A paradigm shift from a screening to a diagnostic capacity requires not only new knowledge and new technology. Equally important is the management of clinical data with feature extraction to provide user support, identify shortcomings and stimulate learning in a wide sense. All of these are necessary to enable accurate and safe usage of the routinely available FECG signal during the most high risk situation – the delivery.

Background

Intrapartum monitoring technologies

Recording the fetal heart rate (FHR) has been standard clinical practice for more than 150 years. The wooden Pinard's stethoscope was the first technology to be introduced and is still in clinical usage by labour staff. However, it only provides intermittent information on the number of heart beats per minute. A fetal scalp electrode was developed in the beginning of the 1960s and allowed for a continuous FHR trace to be recorded during labour after rupture of membranes. It was believed that the provision of continuous information would enable clinicians to detect babies exposed to oxygen deficiency. Electronic fetal monitoring (EFM) was developed with the introduction of cardiotocography (CTG) technology, which rapidly gained clinical acceptance and commercial success.

In many countries, information on the status of the fetus during delivery has up until now been obtained using CTG alone or with the addition of fetal blood sampling (FBS) or fetal pulse oximetry.

Cardiotocography, CTG

Since its introduction in the early 1970s, CTG monitoring of the fetus has become standard clinical practice. CTG is the continuous recording of FHR and uterine activity. The FHR can be recorded either by direct application of a fetal scalp electrode or from an ultrasound transducer positioned on the abdomen of the mother. Uterine activity is assessed from either a transducer placed on the abdomen of the mother or by placing a pressure sensitive catheter alongside the fetus in the uterine cavity. The healthcare provider visually assesses the recording in order to identify situations of oxygen deficiency.

Since the introduction of CTG monitoring relatively little has been added to the understanding of the physiological mechanisms involved in FHR changes related to fetal hypoxia. The benefit of CTG is to identify the normal progress of labour. However, 30 to 40% of fetuses may display CTG changes that require further analysis and expertise to interpret (Steer *et al* 1989). Even with such expertise, cases are missed, as measurement of the FHR alone does not have the capacity to provide information as to what extent the fetus is adapting normally during the labour process. This may mean unnecessary interference with normal labour, such as FBS or emergency operative deliveries (such as Caesarean section (CS), vacuum extraction (VE) or forceps deliveries), which may result in an increased health risk for mother and fetus and an increase in healthcare expenditures.

Fetal blood sampling (FBS)

The FBS technique involves taking a sample of blood from the fetus by puncturing the fetal scalp whilst in the birth canal and measuring the pH/lactate of the blood. This method of fetal monitoring was introduced at the same time as EFM. FBS is not in general use in many countries and the technique does not provide information on a continuous basis and is cumbersome to perform. However, it is still to be regarded as the reference method to indicate the need for intervention and immediate delivery. These qualifications have been reached with few studies to validate its relationship to perinatal asphyxia (NICE 2007).

Fetal pulse oximetry

Fetal pulse oximetry focuses on recording the actual level of fetal hypoxemia (reduction of oxygen in the arterial blood). Current literature shows diverging views on the usefulness of the information made available from fetal pulse oximetry during labour. Two randomised controlled trials (RCT) have been performed. The first trial was only powered enough to allow for assessment of reduction in CS for non-reassuring fetal status. This was achieved but the overall CS rate did not decrease and the issue was raised why CS for failure to progress (FTP) would increase and a second RCT was undertaken. This study was ended prematurely as an interim analysis showed very high CS rates and no improvements (Bloom *et al* 2006).

Perinatal outcome

For many years, it was assumed that birth asphyxia was the principal cause of cerebral palsy (CP). Indeed, when CTG was introduced in 1970s it was hoped that this technique would reduce the incidence of CP and mental retardation by 50%. Disappointingly, the results of randomised trials showed little or no benefit with respect to long-term neurological outcome, despite widespread use of the CTG (Afirevic *et al* 2006). Studies have shown that around 3-28% of cases of CP are associated with intrapartum asphyxia (Nelson 203).

The CTG is an integral part of intrapartum care in most delivery wards and it is helpful in identifying asphyxiating conditions during labour in a small group of babies at risk of death or irreversible brain injury. CTG remains the central documentary evidence of all claims for fetal asphyxia. In a review of 110 cases of obstetric litigation for CP, Symonds and Senior (1991) found that 70% of these claims were based on abnormalities of the CTG and their interpretation.

An effect of the increasing number and costs of obstetric claims has been an escalating number of CS performed. During the last ten-year period, CS rates in England have doubled to approximately 20% of all deliveries. When questioned in a survey (Churchill *et al* 2006), 47% of obstetricians attributed the rise in the CS rate to 'medico-legal-reasons'. According to another survey, 82% of physicians gave avoidance of medical negligence claims, as a reason for adopting procedures such as CS (Jones and Morris 1989).

EFM is applied in 75% of deliveries (Boehm 1999) in the US and there is evidence to show that the operative delivery rates are significantly increased with the use of EFM especially if FBS is not used as an adjunct to establish the fetal condition (Thacker *et al* 2001). The UK fourth 'Confidential inquiries into Stillbirths and Deaths in infancy'(1995) analysed the intrapartum deaths that were due to asphyxia in babies greater than 1500 g with no chromosomal or congenital malformation. The conclusion was that 50% of the deaths could have been avoided if an alternate care had been provided. The reasons identified for the poor outcomes were; inability to interpret CTG, failure to incorporate the clinical picture, delay in taking appropriate action and poor communication. This is not entirely surprising as the model of FHR interpretation is largely based on empirical observations of thousands of hours of recordings during human labour (Hon 1967). Large intra-and inter-observer differences in the interpretation of CTG recordings have been reported and even amongst experts (Nielsen *et al* 1987, Donker *et al* 1993, Bernardes *et al* 1997).

In their recent analysis, Amer-Wählin and Dekker (2008) states that CTG will always be a nonspecific method, currently dependent heavily on subjective interpretation. Thus, the labour ward staff (and the fetus) remains at risk for wrong or delayed action as clear-cut information is not available. Only with the addition of non-subjective information will the risk decrease.

Acid Base

A central component in any attempt to reassess quality of care is the availability of marker of potentially adverse outcome. The choice of a marker has to be done with care. It has to be possible to obtain the information routinely, preferably during the perinatal period. It should have a high specificity and a 'reasonable' prevalence. From these prerequisites follows that outcome measures such as perinatal mortality, CP rates and even hypoxic ischemic encephalopathy (HIE) would be too rare and require too many resources to be obtained. Umbilical cord acid-base analysis has become part of routine care and serves as a quality measure as well as to provide risk assessment.

Acidosis and neurological symptoms during the neonatal period

In a study by Low *et al* (1994) as many as 61% of 59 term infants with metabolic acidaemia (buffer base <30 mmol/l) had encephalopathy. In a Swedish study (Ingemarsson *et al* 1997) ten of 154 infants (6.5%) with umbilical artery pH <7.05 had neonatal cerebral complications, comparable with the rate in a study by Fee *et al* (1990), where six of 110 infants with cord artery pH <7.04 had encephalopathy. In a study by Nagel *et al* (1995) 30 infants with cord artery pH <7.0 were followed up for one to three years. Of the 28 infants who survived the neonatal period, only one had a mild motor developmental delay. Dennis *et al* (1989) compared infants with acidaemia at birth with non-acidotic babies having normal Apgar scores, and with low Apgar scores, for performance in neuro-developmental tests at age 4.5 years. They found no association between acidosis and neuro-developmental function in

contrast to the findings of Ingemarsson *et al* (1997).

The reason for the discrepancy may be related to the cause of the development of acidaemia and acidosis. The appearance of a metabolic or respiratory acidaemia is a consequence of a decrease in placental blood flow with decreased gas exchange. A respiratory acidaemia is caused by a decrease in the transport of carbon dioxide (CO₂) from the fetus to the mother. CO₂ is produced in large amounts in the cellular energy yielding metabolic processes and a continuous placental blood flow is required to avoid CO₂ accumulation. If this occurs, CO₂ is converted to hydrogen ions, some of which become free and will cause a rapid decrease in pH and a respiratory acidaemia.

Metabolic acidosis should be regarded as an active response to hypoxia, whereby anaerobic metabolism generates lactic acid. From this process, the acid component – the proton (H⁺) is buffered in the tissues and the base – lactate accumulates until it gets metabolised.

Respiratory and metabolic acidaemia has different origins and means different things to the fetus. A respiratory acidaemia belongs to normal delivery; it emerges rapidly and disappears rapidly with the first few breaths of air. Very high CO₂ concentrations may delay the onset of spontaneous respiration.

Metabolic acidaemia carries a risk for the tissues being affected. Metabolic acidaemia requires time to develop and it remains for longer periods of time. Furthermore, repeated episodes may add to each other thereby causing a reduction in the safety margins with a decrease in buffering capacity.

Metabolic acidosis is calculated from algorithms using pH and pCO₂. There are two alternatives (Figure 1), the first developed by Siggaard Andersen in 1963, the Alignment nomogram where base deficit (BD_{ecf}) was calculated using the blood buffers only. This algorithm was found to overestimate the metabolic acidosis component in case of a mixed acidaemia. A second algorithm was therefore presented in 1971 (Siggaard-Andersen 1971), the ‘Acid-Base Chart’ where changes in extra-cellular fluid (ecf) buffers were calculated, thereby avoiding the impact of a respiratory acidosis (always accompanying an umbilical cord metabolic acidosis) on BD_{ecf} calculations. Figure 2 illustrates the principles of acid-base alterations in connection with the development of respiratory acidaemia. The increase in plasma bicarbonate (HCO₃⁻) causes a shift into the extravascular space and a loss of buffers from the blood compartment. By definition this would mean metabolic acidosis in the blood compartment, corrected for by including the whole extracellular space in the calculation of buffer distribution. Unfortunately, commercially available blood gas machines have not adopted Siggaard-Andersen ‘Acid-Base Chart’ algorithms.

Acid-base Chart

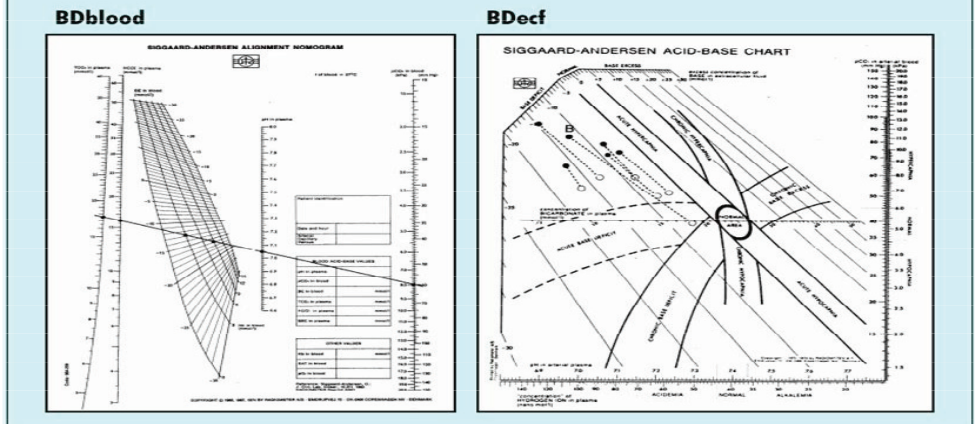


Figure 1. The two Acid base charts developed by O Siggaard-Andersen.

The implication of this is that metabolic acidosis in newborn becomes more frequent as a high $p\text{CO}_2$ will cause a falsely low base excess (Rosén and Murphy 1991).

The cut-off point for pathological fetal acidaemia correlating with an increasing risk of neurological deficit has been set to a pH of less than 7.00 and a base excess (BE) of less than -16 mmol/l (Goldaber *et al* 1991, Winkler *et al* 1991). In the literature, the level mostly used as diagnostic criterion is 12 mmol/l (Maclennan 1999). If umbilical blood or neonatal blood gas data do not exist, it is impossible to be certain of a causative mechanism. If records of both arterial and venous umbilical gases exist, then a difference in BD_{ecf} of >3 mmol/l suggests an acutely developed metabolic acidosis with the artery having the highest BD_{ecf} (Sundström *et al* 2000).

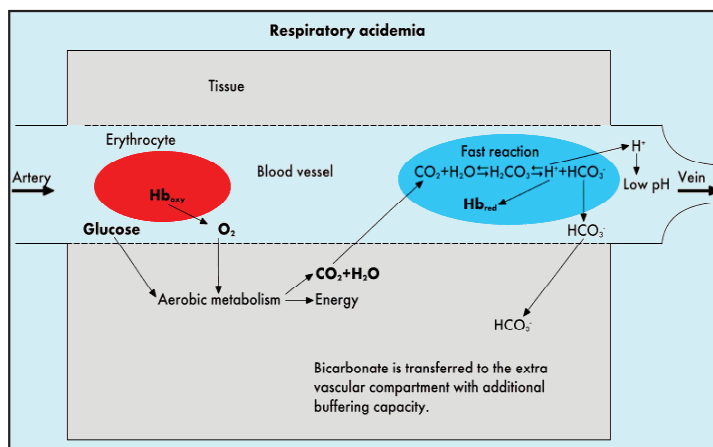


Figure 2. Principles of acid-base changes in connection with respiratory acidaemia. Modified from Sundström *et al* 2000.

Assessment of acid base data

The process of obtaining and analyzing cord samples for acid base data analysis have previously been validated (Westgate *et al* 1994) and methodological issues have been identified. One such area is erroneous $p\text{CO}_2$ readings. A falsely low $p\text{CO}_2$ will cause a falsely high calculated BD_{ecf} . The simplest way to determine the accuracy of a set of cord samples is to verify that the cord artery sample (lowest pH) should always have the highest $p\text{CO}_2$. If that is not the case, the sample will not accurately reflect the acid base status.

In case the cord samples are accurately obtained, BD_{ecf} in the artery and vein may be used as markers of the duration of hypoxia (Westgate *et al* 1994). A high BD_{ecf} in the cord artery but a normal in the cord vein would indicate a short lasting hypoxic process. When both the artery and vein indicate metabolic acidosis, an increased risk for neonatal symptoms and persistent hypoxic tissue damage would be expected.

Hypoxia is associated with a decrease in placental blood flow, and as a consequence there may be situations where blood is available in the vein only. A cord vein sample indicating metabolic acidosis should be regarded as a significant finding.

Obviously there are situations where no cord data are available at all, but still the newborn is affected by hypoxia and metabolic acidosis. These are cases where the newborn shows low Apgar at 5 minutes, requires active resuscitation, and shows metabolic acidosis/lactate rise in samples obtained immediately post partum. Furthermore, these neonates have clinical symptoms and often require buffering.

In summary:

- For an unaffected newborn to be diagnosed with sustaining metabolic acidosis, both cord artery and vein samples are required with the cord artery sample showing a lower pH and higher $p\text{CO}_2$.
- In case only one sample is available, it should be treated as a venous sample and in case of metabolic acidosis the sample indicates a more substantial risk.
- Even in case of no cord acid base data being available, the newborn may still be diagnosed as having metabolic acidosis, provided it is affected and there are acid base data or lactate data obtained within the first hour to indicate metabolic acidosis.

Neonatal metabolic acidosis is defined as newborns with metabolic acidosis (cord sample or immediate neonatal finding) where the infant has developed symptoms (neurological, cardiorespiratory, metabolic) requiring special neonatal care.

Considerations when analyzing outcome

Consensus has been reached regarding the basic requirements for the diagnosis of intrapartum asphyxia (MacLennan 1991) Cord artery metabolic acidaemia of $\text{pH} < 7.00$ and base deficit ≥ 12 mmol/l is defined as a biochemical marker of asphyxia. Unfortunately, this international consensus statement does not specify what base deficit algorithms should be used.

The BD_{ecf} estimation of metabolic acidosis and the chosen cut-off of cord artery $pH < 7.05$ and $BD_{ecf} > 12$ mmol/l has been used in most of the research on ST analysis performed after 1991. This identifies fetuses with a significant metabolic adjustment to hypoxia without being clinically affected, and serves as a relevant biochemical marker. It was confirmed in the Nordic study where ten of the 15 fetuses with cord metabolic acidosis had normal neonatal periods (Amer-Wählin *et al* 2002). The range of cord artery pCO_2 readings showed that the metabolic acidosis was always combined with a respiratory acidemia, thus verifying the importance of using BD_{ecf} algorithms including buffer distribution in the whole of the ecf -compartment.

Additional information and analysis of the FECG bioprofile

The aim of fetal monitoring during labour is to identify fetuses at risk of an adverse outcome based on our ability to understand what is happening and how the fetus reacts to stress before it becomes a risk situation. It is only when adverse events and patterns can be accurately understood and analysed, that there is an opportunity to improve data interpretation clinically.

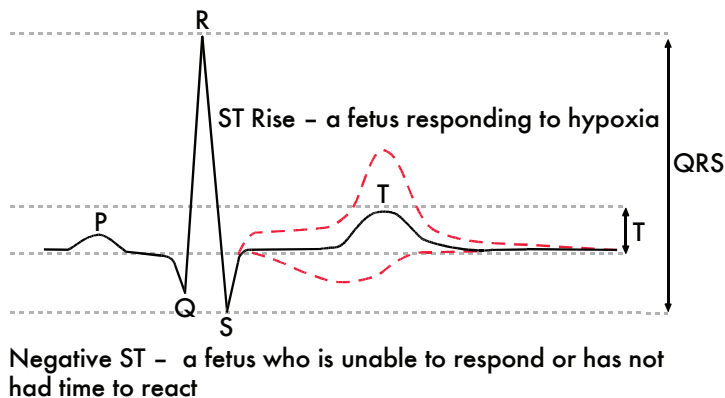


Figure 3. A sequence of the fetal ECG including its components and their physiological relevance.

The fetal ECG and its physiology

The ECG reflects the summation of electrical events within the myocardial cells, as recorded from the body surface. Electrical changes seen on the surface occur in relation to changes in action potentials in the ventricular myocardium over time. In a normal healthy myocardium, the cells are in a polarized state (i.e. equal number of positive and negative charges) during diastole with an accumulation of positive charges, which is balanced by an equal number of negatively charged ions, extracellular electrons. This is the normal resting state until depolarization occurs. At this point the distribution of negative and positive charges is reversed by a self-propagating wave from cell to cell through a 'battery condition'; if the outer cell is positive and its adjacent cells are negative a local current will flow. The P and QRS

waves (Figure 3) are the resulting electrical activity produced by the propagation of the depolarisation wave. The T wave represents the time difference between repolarisation of different parts of the myocardium.

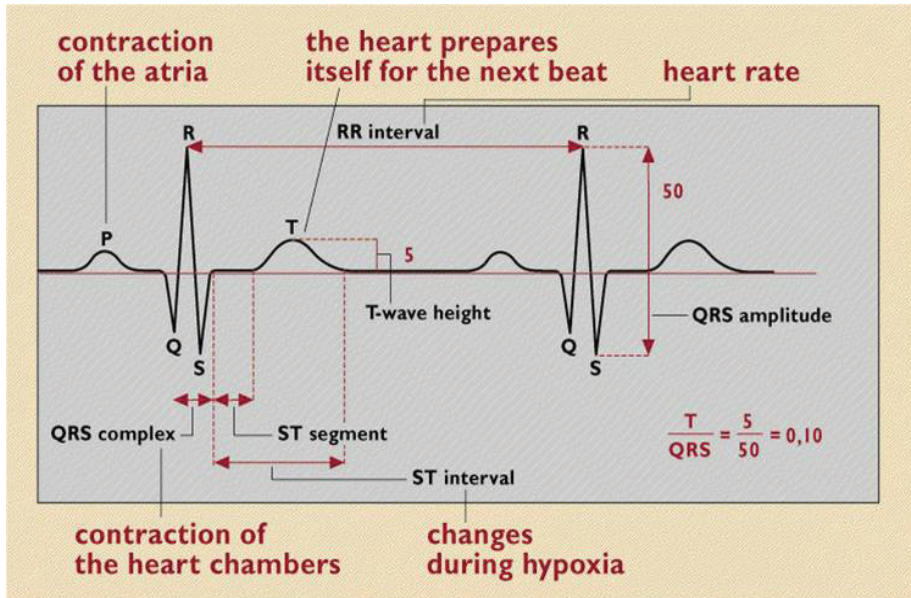


Figure 4. Principles of how to calculate the T/QRS ratio and the physiology behind different ST patterns.

The sino-atrial node controls the action of the heart and the cells in this node are controlled by vagal and sympathetic nerves as well as by hormones such as adrenaline. The P wave configuration and time constants are affected by changes in the autonomic nervous system controlling part of the heart pump function. The P wave of the ECG (Figure 4) corresponds to the contraction of the atrium. The next sequence is the contraction of the ventricles, represented by the waves Q, R and S. The generation of these waves is a passive event and thus very stable and easily detected which makes it well suited for FHR recording.

The significance of FECG changes

PR time interval

Hypoxia may cause an alteration in the PR time with a PR shortening in spite of a RR lengthening, but this is more related to the fetal heart attempting to preserve an optimal filling of the atrium in situations of a decrease in blood returning to the heart (Widmark *et al* 1992, Luzietti *et al* 1997). The significance of a sequence of PR shortening in connection with a lowering of the heart rate (bradycardia) would be to identify a vagal dominance in contrast to a direct depressive hypoxic effect.

Q-T time interval

In intrapartum hypoxia, resulting in metabolic acidosis, a significant shortening of the fetal QT interval is present, also when the QT time is corrected for changes in heart rate. The observation of a shortening QT interval during hypoxia provides us with additional information on the condition of the fetal myocardium and the ionised calcium fraction affecting the pumping function (inotropic response) of the working heart (Oudijk *et al* 2004).

ST changes

The ST segment and T wave relate to the repolarisation of myocardial cells in preparation for the next contraction. This repolarisation process is energy consuming. An increase in T wave height occurs when the energy balance within the myocardial cells is threatened. During hypoxia this balance becomes negative and the cells produce energy by the β -adrenoceptor mediated anaerobic breakdown of glycogen reserves. This process not only produces lactic acid but also potassium ions (K⁺) which affect myocardial cell membrane potential and cause a rise of the ST waveform (Fenn 1939).

When energy balance cannot be maintained by vasodilatation or anaerobic metabolism, ischemia occurs in the endocardium. This will alter the sequence of repolarisation changing myocardial cell potentials and thus the direction of the current flow. A depression of the ST segment with or without negative T wave will occur (Figure 3) (Wohlfart 1987).

The maintenance of fetal myocardial function and survival during hypoxia depends on myocardial glycogenolysis as described by Dawes *et al* (1959). With increasing glycogenolysis, there is a further increase in T-wave amplitude (Rosén and Isaksson 1976) and the correlation between the rates of glycogenolysis and increase in T/QRS has been described as linear (Hökegård *et al* 1981).

Role of β -adrenoceptor activation

Apart from hypoxia, myocardial glycogenolysis could be activated pharmacologically by administering β -adrenoceptor activating agents enhancing myocardial work performance. The relationship found between increase in myocardial work during hypoxia and the T wave height is illustrated in Figure 5.

An important aspect of fetal response to hypoxia is the marked surge of catecholamines. Figure 6 shows the observations made in relation to the level of acidaemia, concentrations of catecholamines and T/QRS. Thus, it appears as if during moderate hypoxemia the appearance of an increase in T wave amplitude is related to the adrenaline surge, β -adrenoceptor activation and myocardial glycogenolysis and indicating fetal myocardial metabolic reactivity.

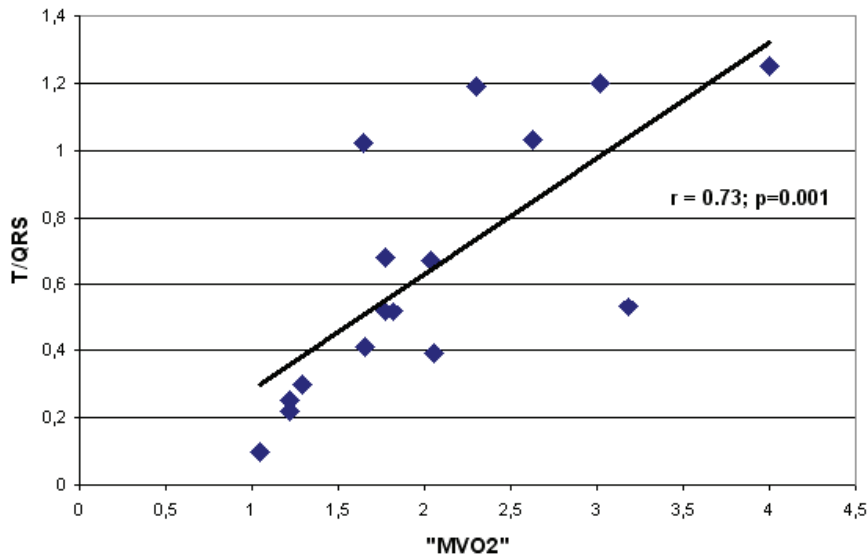


Figure 5. A plot of T/QRS and myocardial work load index data in the fetal sheep obtained during hypoxia in connection with exogenous β -mimetic (terbutaline) infusion to the ewe. 'MVO₂' defined as mean arterial blood pressure x cardiac output x myocardial contractility (max dP/dt) (Dagbjartsson *et al* 1989).

ST depression/negative T waves indicates an imbalance between endo- and epicardium: the perfusion pressure of the endocardium is always the lower at the same time as the mechanical strain is always the larger causing delay in the repolarisation (recovery) phase. This means that unless the myocardium is generally activated (β -receptor activation and enhanced Frank-Starling relationship, i.e. the ability of the myocardium to respond to volume load), a decrease in performance for whatever reason, may cause ST depression. Thus, not only hypoxia per se may cause ST depression as a sign of mal-adaptation, but also factors substantially altering the balance and the performance characteristics within the myocardial wall. So far a number of clinical situations have been associated with ST depression/negative T waves such as prematurity, infections, maternal fever, myocardial dystrophy and cardiac malformations (Rosén 2001). Yli and colleagues have recently documented the more frequent occurrence of ST depression in fetuses from mothers with diabetes mellitus, a disorder known to be associated with fetal myocardial dystrophy (Yli *et al* 2008).

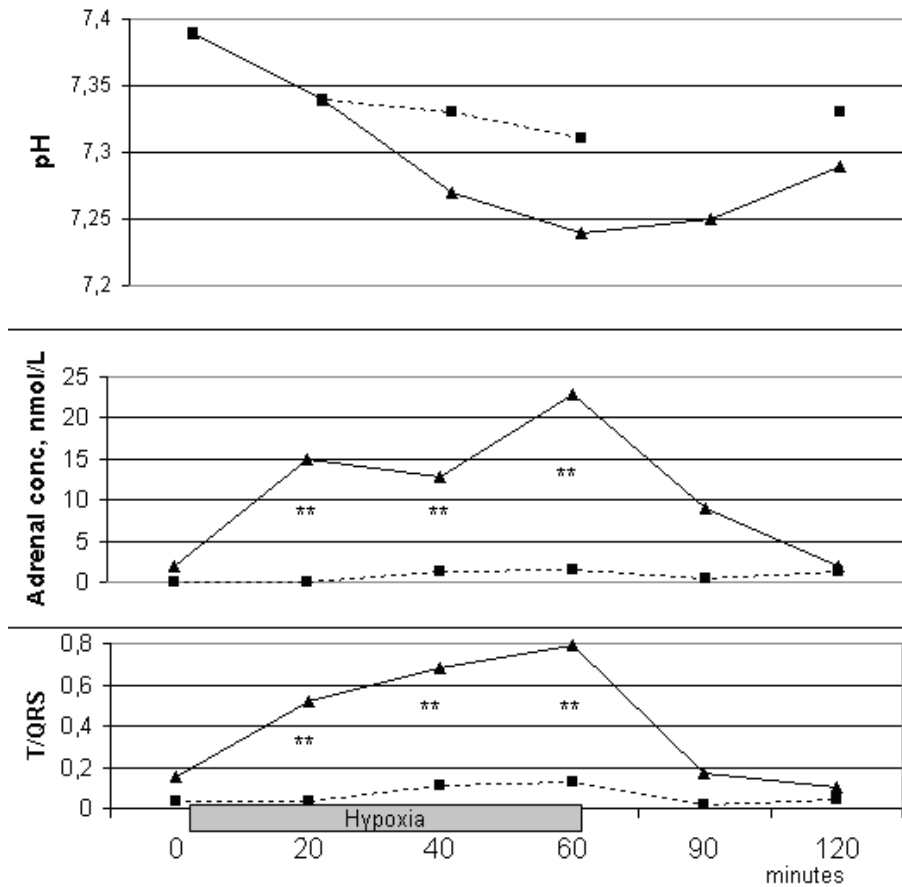


Figure 6. Changes in artery pH, plasma adrenaline concentration and T/QRS in connection to 60 minutes hypoxia induced by letting the ewe breath a 7% oxygen gas mixture. Solid lines indicates the group of fetuses (n=10) that responded with an increase in T wave amplitude and dashed lines indicate group of fetuses with no ST change in response to hypoxia. The level of significance between the groups are indicated (** $p < 0.01$). Data modified from Rosén et al 1984.

The relationship between gestational age and hypoxia have recently been elucidated by Mallard's group, by observing the type of ST patterns emerging in connection with cord occlusion and endotoxin administration in the mid gestation fetal lamb (Welin et al 2005). During prolonged cord occlusion, the mid-gestation fetal sheep has the capacity to react to asphyxia with a significant increase in the amplitude of the ST wave form together with an augmentation of blood pressure, which then subsides as the asphyxia continues. The appearance of negative ST segment appears to signify significant cardiac dysfunction with hypotension. The same group has recently been able to study the impact of endotoxemia (Blad et al 2008). The responses to lipopolysaccharide endotoxin developed gradually over several hours and were the opposite of those after asphyxia (hypotension, tachycardia and ST depression/negative T waves). The ST depression/negative T wave changes may represent reduced capacity of the myocardium to serve as a pump

Principles of alterations in the Frank-Starling relationship with immaturity, hypoxia and infections

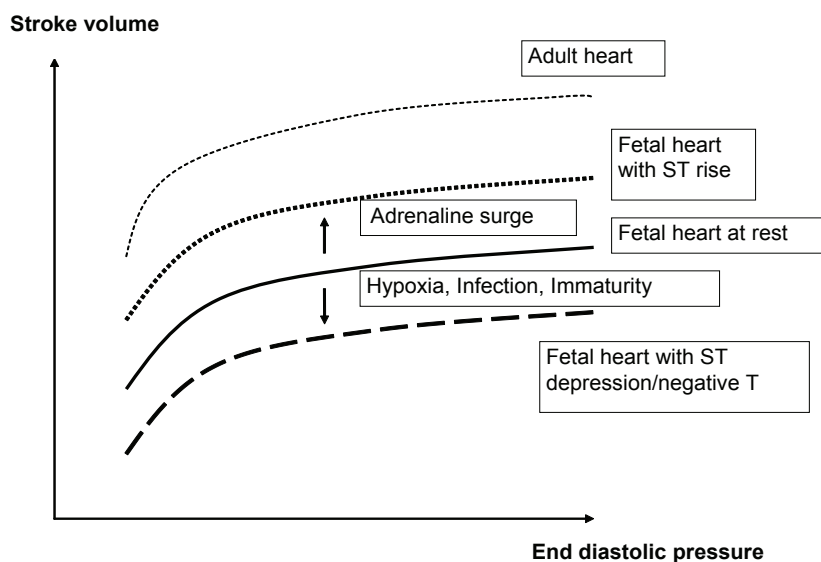


Figure .7 Illustrations of changes in the Frank-Starling relationship in connection with different ST patterns (Rosén, personal communication).

Identification of specific clinical guidelines and construction of systems to support the clinician

The initial phase of the clinical work with ST analysis between 1979 and 1989 focused on the verification of the experimental findings. Mode of recording the FECG as well as the relationship to biochemical markers was investigated. Lilja *et al* (1985) showed that two scalp electrodes provided a sufficiently stable signal and a linear correlation was found between T/QRS ratios obtained within 30 minutes of delivery and cord lactate values ($r=0.58$, $p<0.01$).

An important aspect was the identification of index cases, e.g. cases that developed signs of hypoxia, and the extent to which ST waveform changes would also be present. Figure 8 shows a recording from one of the index cases of intrapartum hypoxia displaying a marked rise in T wave height and T/QRS ratio during second stage of labour. A combination of respiratory and metabolic acidosis can be noted.

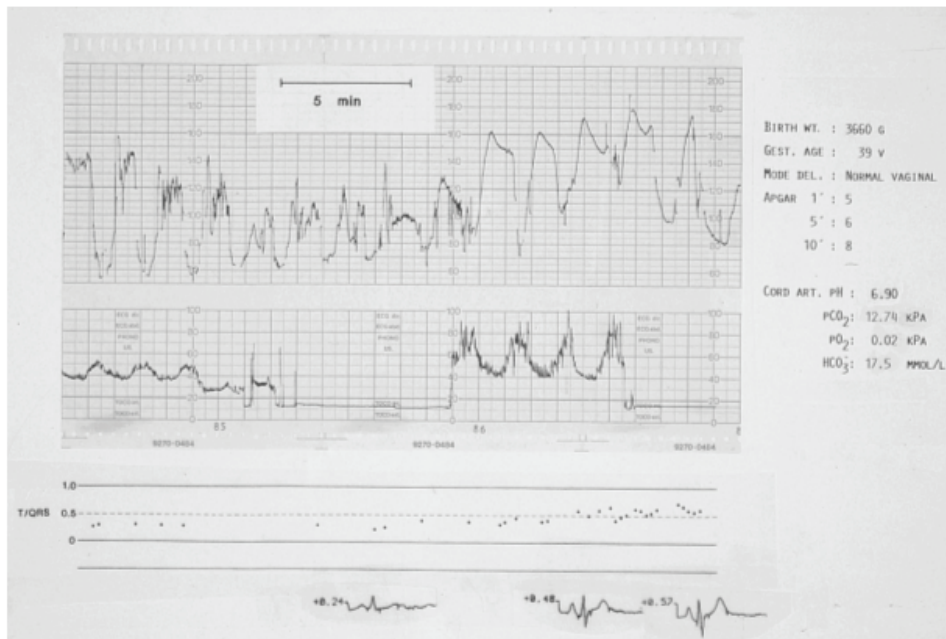


Figure 8. A sample of a combined CTG +ST analysis prototype recording showing an increase in T/QRS ratio with abnormal CTG patterns. Recording obtained by H Lilja, Sahlgren's University Hospital, Göteborg in 1987.

The technology applied in these early stages has been described by Rosén and Lindcrantz (1989). Despite the limitations in signal processing capacity it was shown that the ST analysis model of recording and processing the FECG provided ST waveform changes identical to those recorded during experimental hypoxia. These findings were further analysed by Arulkumaran *et al* (1990). Of 201 patients recorded during labour, nearly 45% had suspicious or abnormal FHR traces while only 27% had T/QRS ratio greater than 0.25 (mean +2 SD). A normal T/QRS ratio identified 99% of fetuses with normal buffering capacity in cord artery blood. Acute hypoxia was recognized by the rapid rise in T/QRS. It was also shown that the specificity of T/QRS to identify fetuses at risk increased by combining the ST waveform analysis with FHR changes.

These data formed the basis for the first CTG+ST clinical guidelines, refined and validated in the Plymouth RCT (Westgate *et al* 1993). The guidelines contain the combination of CTG and ST analysis. The experimental data had clearly shown that ST analysis on its own provided information on the ability of the fetus to handle hypoxia. At the same time experimental data had also shown that β -adrenoceptor activation without hypoxia could institute ST elevation and it appeared logical to assume that there would be instances where the external forces (squeezing and squashing) during labour would cause catecholamine release, increased T/QRS ratio and a very reactive CTG with no evidence of intrapartum hypoxia.

These early studies also showed that the fetal reactions to hypoxia vary over time and a fetus exposed to long-term hypoxia may react differently as compared to the previously healthy fetus exposed to an acutely emerging hypoxic episode during second stage of labour.

Furthermore, the fetal adaptation to chronic hypoxia means a gradual decrease in fetal reactions. The same vigour in the adaptive changes in the myocardial metabolism with a long lasting hypoxic event as compared with an acutely emerging event should not be expected. In such a situation, a CTG pattern without any signs of reactivity and heart rate variability, i.e. a preterminal trace, would be the most relevant finding.

It is also possible for a fetus down regulating its activities (hibernating) in response to a long-term stress in which case the loss of signs of FHR reactivity would be the expected finding with little or no ST changes.

Cord artery pH is a robust parameter that has been shown not to have a normal distribution, as there is a cohort of babies in the low pH range (Westgate and Greene 1994). It appears as if this cohort may be identified from CTG+ST analysis. Data from the Plymouth RCT (Westgate *et al* 1993) showed that cases with ST elevation and abnormal CTG all had cord artery pH ≤ 7.15 . In the Nordic observational study (Amer-Wählin *et al* 2002), 86% of the cases where the CTG+ST clinical guidelines called for intervention, the cord artery pH was < 7.15 . The increased sensitivity to detect a lowering of cord artery pH may be accounted for by the improvements in signal quality and the ability of the technology to more accurately identify ST changes and ST depression at an earlier stage of hypoxia.

The Plymouth RCT (Westgate *et al* 1993) demonstrated that the CTG by itself provided information on the fetal situation in as much as there was a significant decrease in cord artery pH in combination with an increase in severity of the CTG pattern. The pH decreased from a mean value of 7.26 with a normal CTG to 7.21 when the CTG became intermediate and was reduced to 7.14 with an abnormal CTG.

Clinical verification

The Plymouth RCT

With the need to provide scientific evidence of the clinical value of CTG+ST waveform, a large RCT was conducted in the non-academic unit at Freedom Fields Hospital in Plymouth (Westgate *et al* 1993). In 1990, the labour ward in this hospital was one of the largest in England and it was thought to reflect the level of care seen in a busy labour ward. The design and size of the trial was such that no research staff would oversee every case. The ordinary staff handled the cases thereby enabling the trial to better reflect a situation of general clinical use of CTG+ST analysis. Although it was understood that further technological developments would be required, STAN 8801 (Cinventa Medical, Mölndal, Sweden) provided a technique that could be used with appropriate training and motivation.

The trial met with the primary aim of showing a reduction in operative deliveries for fetal distress without increasing the risk of newborns suffering from hypoxia. There was a 46% reduction ($p < 0.001$, odds ratio 1.85 [1.35-2.66]) in operative deliveries for fetal distress (ODFD) and a trend to fewer metabolic acidosis ($p = 0.09$, odds ratio 0.38 [0.13-1.07]) and fewer low five-minute Apgar score cases ($p = 0.12$, odds ratio 0.62 [0.35-1.08]) in the ST+CTG arm.

The trial tested the hypothesis that a combination of CTG+ST analysis compared to CTG only would reduce ODFD without placing the fetus at risk. If the primary endpoint had been to obtain a reduction in metabolic acidosis rate, the 2400 cases enrolled in the trial were not sufficient as 3600 cases would have been required to demonstrate a 50% reduction in cord artery pH < 7.05 and $BD_{ecf} > 12$ mmol/l ($\beta = 0.20$, $\alpha = 0.05$, incidence 1.3%). Thus, the next step in the clinical verification of CTG+ST analysis would be to test the ability to improve outcome by lowering the incidence of metabolic acidosis.

The European Community and Nordic studies

The European Community descriptive multi-centre trial was initiated to validate signal processing (Luzietti *et al* 1999). The STAN 8801 model was used while linked to a computer for data acquisition. Considerable improvements in signal processing occurred after the study was completed, when digital signal processing was introduced.

A second descriptive study in 12 Nordic labour wards (Amer-Wåhlin *et al* 2002) was therefore initiated. It included 574 cases recorded using a new prototype of the STAN monitor (Neoventa Medical AB, Mölndal Sweden) where FECG data was stored for subsequent computerised ST analysis.

In the Nordic study, 15 cases were identified as being exposed to intrapartum hypoxia. Five cases had neonatal neurological symptoms (increased neuromuscular tone: 2 cases, seizures within 24 hours: 3 cases), all had abnormal FECG findings during first stage of labour. Another ten cases had cord metabolic acidaemia only; two had changes in first stage of labour and the remaining eight showed ST changes during active pushing in second stage only.

An increase in baseline T/QRS occurred in 12 of the 15 cases exposed to intrapartum hypoxia. The range of increase in baseline T/QRS was 0.07 to 0.20 with an average increase of 0.13. One case displayed an episodic increase in T/QRS during the last nine minutes of labour; one case showed consistent ST depression with negative T waves and the final case had a preterminal CTG. Thus, the CTG+ST clinical guidelines were found to provide adequate support in identifying intrapartum hypoxia.

The Swedish RCT

The aim of the Swedish RCT (Amer-Wählin *et al* 2001) was to verify the ability of the CTG+ST to improve neonatal outcome by lowering the incidence of metabolic acidosis. The Plymouth RCT (Westgate *et al* 1993) was a single centre study, but the Swedish trial was designed as a multi-centre trial in three busy labour wards.

The trial included 4966 women with term fetuses in cephalic presentation during labour after a clinical decision had been made to apply a fetal scalp electrode for internal CTG recording. Patients were randomised to CTG+ST analysis or to CTG only. The trial was designed with a power to assess potential improvements in neonatal outcome. The design also allowed testing for the effects of growing experience with the new ST analysis technology in the three labour units with cases managed by more than 300 midwives and physicians.

Table I shows the outcome with regard to the primary aim of the trial, a more than 50% reduction in cord artery metabolic acidosis. When the basic recommendations of starting a recording in first stage of labour and maintaining data collection within 20 minutes of delivery ('adequate recordings') were followed, further improvements were noted.

Mode of analysis	CTG+ST	CTG	OR, 95% CI, p-value
Intention to treat	15 0.69%	31 1.49%	0.46 0.25-0.86 0.02
No of cases	2159	2079	
Adequate recordings	11 0.57%	27 1.44%	0.39 0.19-0.79 0.01
No of cases	1926	1871	

Table I. Numbers and rates of cases with cord artery metabolic acidosis.

The trial showed a significant reduction in operative ODFD from 9.3% to 7.7% (OR 0.81, $p=0.047$). Table II shows the ODFD rates related to the two phases of the trial. It was only with growing experience and the introduction of structured case discussions during the second phase of the trial that a positive effect on ODFD rates was noted.

The main aim of the trial was to show improvements in neonatal outcome using cord artery metabolic acidosis as a marker of adverse situations. The reason for choosing a marker such as BD_{ecf} has previously been discussed in this thesis. During the second phase of the trial, a reduction in cord artery metabolic acidosis from 1.48% to 0.50% was noted (OR 0.33, $p=0.045$).

Intention to treat	CTG+ST	CTG	OR, 95% CI, p-value
First phase	114 8.6%	104 8.3%	1.03
No of cases	1333	1250	
Second phase	79 6.7%	123 10.3%	0.62 0.46-0.85 0.002
No of cases	1186	1197	

Table II. Numbers and rates of cases with ODFD. Separation of data according to mode of monitoring and phase of the trial.

Neonatal outcome

In the Swedish RCT (Amer-Wählin *et al* 2001), neonatal metabolic acidosis was defined as newborns with metabolic acidosis (cord sample or immediate neonatal sample) where the infant developed symptoms (neurological, cardio-respiratory, metabolic) requiring special neonatal care. The size of the trial allowed an assessment of outcome related to monitoring among the 351 babies that were admitted to the Special Care Baby Unit (SCBU).

In a follow-up study, the assessment of the clinical data was made by an experienced neonatologist who had no knowledge of which group of monitoring the case belonged to (Norén *et al* 2003). From the 351 cases, 29 were identified as having an adverse outcome related to labour and delivery. No difference between the two arms occurred during the first phase of the trial. Only when CTG+ST guidelines were followed more accurately with growing experience in the second phase of the trial, could a significant reduction in adverse outcome cases be noted from 1.0% (12/1197) to 0.17% (2/1186) in the CTG and CTG+ST arms, respectively.

The main aim of fetal surveillance is to minimise the risk of neonatal morbidity and mortality. The trial (Norén *et al* 2003) documented a significant reduction of moderate or severe neonatal encephalopathy in term newborns with a reduction from 3.3‰ to 0.4‰ (OR 0.12, 95% CI 0.01–0.94, $P < 0.02$).

There is a host of evidence to support the use ST waveform analysis as an adjunct to CTG monitoring from pre-clinical animal studies and RCTs. Nevertheless, there is still a need to explore the improvements in neonatal outcome in regular obstetric care as illustrated by the concept of phase IV studies. This aspect will be the focus of this thesis.

Aims of the thesis

The overall aim of this thesis was to evaluate the ST waveform analysis of the fetal ECG as an adjunct to standard CTG as a new method for intrapartum monitoring and as part of regular obstetric care. More specifically:

- To evaluate whether the addition of ST waveform analysis of the fetal ECG will increase the ability to detect fetal intrapartum hypoxia and more appropriately intervene in cases of documented hypoxia and metabolic acidosis.
- To analyse change occurring over time during the introduction of the ST waveform analysis in regular care.
- To test the hypothesis that CTG+ST clinical guidelines will identify cases of intrapartum acidosis with accuracy similar to that of CTG+FBS.
- To undertake detailed analysis on the timing of CTG, FBS and ST changes as part of a case control study of cord artery acidosis.
- To investigate the usage of FBS in connection with CTG+ST recordings.

Material and methods

General aspects

All papers included in the thesis contain clinical data originating from labour wards across Europe and serve to provide information collected as part of the introduction of ST waveform analysis. The European Union ST analysis trial was a prospective multi-centre observational study funded by the European Union that involved ten European University hospitals studying the clinical implementation of ST analysis. Ethical approval and informed consent was obtained in those centres where ST analysis was not yet part of standard care.

The ‘City of Göteborg study’ (**Paper I**) was conducted as part of the European Union ST analysis trial between October 1 2000 and September 30 2002. This study contained data from 14687 term pregnancies in active labour.

Detailed analysis of FBS, ST and FHR data (**Papers III and IV**) were conducted on a subset of 194 cases originating from the European Union ST analysis trial. This material included 6999 cases, all recorded in centres using FBS as an adjunct to standard CTG monitoring. An FBS was obtained in 911 cases of which all cases with cord artery pH <7.10 and corresponding controls were included in the analysis presented in **Papers III and IV**.

Paper III served as an observational study providing detailed analysis of cases with marked acidosis. In **Paper IV**, the analysis was extended into a case controlled study including cases with both acidaemia and acidosis.

Additional to the ‘City of Göteborg study’ covering the total population of term deliveries in a University hospital setting, the outcome of two years of regular usage of CTG+ST analysis in a district hospital, was also audited (**Paper II**). These data include 3193 term deliveries from the city of Varberg, located on the west coast of Sweden.

In total 18791 term deliveries, defined as >36 completed gestational weeks, have contributed to the data analysis in this thesis, 7616 monitored with CTG+ST and 11175 with CTG only.

STAN Fetal heart monitor

When FECG is recorded with a scalp and a skin electrode, changes in the T wave and the ST segment of the FECG are automatically identified and analysed by the application software. The STAN system calculates an average ECG waveform from the FECG channel (scalp-to-skin lead). Every fetal heartbeat generates an FECG complex, which is assessed by the STAN monitor against strict quality criteria. The averaging is performed over 30 consecutively qualified FECG complexes. The device uses the average ECG waveform to process the T/QRS ratios, i.e. the ratio between the T-wave amplitude and the QRS-complex amplitude. A T/QRS baseline is computed every minute and monitored for multiple characteristics, contributing

to a determination of a T/QRS difference and the identification of a significant T/QRS change constituting an event (Table IV). The initial 20 T/QRS ratios are used to collect T/QRS baseline data to allow for an accurate determination of starting values used by the processing algorithms for event detection.

The analysis is displayed in the lower section of the STAN screen as a series of data points (T/QRS crosses) and event markers. The ST analysis identifies patterns and changes in the T wave and ST segment over time, and displays events based on the analysis of those changes. All events are stored in the event log. The user considers their interpretation of the standard CTG parameters together with the ST analysis results, and CTG+ST clinical guidelines help the labour ward staff to decide what action should be taken clinically in relation to CTG changes and ST events.

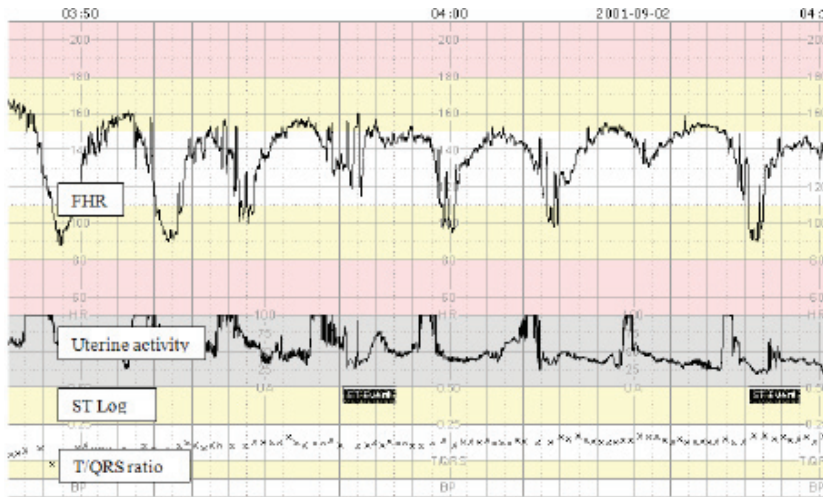


Figure 9. STAN recording showing a marked increase in beat-to-beat variation associated with a progressive baseline T/QRS rise (ST events) of 0.06 at 09:58 and 0.11 at 10:07, normal vaginal delivery at 11:19, Apgar scores 3-5, cord artery pH 6.97, BD_{cef} 18.0 mmol/l.

The STAN software conditions and analyses the raw FECG signal to identify characteristic parameters of the T wave and QRS complex used to calculate the T wave and QRS complex amplitudes and the T/QRS ratio. The decision algorithm evaluates these parameters looking for the three types of events: (1) episodic T/QRS rise, (2) baseline T/QRS rise; and (3) biphasic ST. The method defines biphasic ST as a condition where the slope of the ST segment has become negative, which the decision algorithm uses as an indicator of fetal abnormality. Biphasic events are further classified into category 1, 2, or 3 indicating that the slope is above baseline, crossing the baseline, or below baseline, respectively.

STAN recordings are automatically given a separate identification number at time of the recording. In the Varberg labour ward audit (**Paper II**), these unique case numbers were associated with patient ID numbers used in the hospital based patient database (Obstetrix, Siemens AB). Clinical data were obtained from the information collected as part of the Swedish National Perinatal Registry. Retrospective assessment

of STAN recordings of cases with ODFD and acidaemia (cord artery pH <7.05) were made to assess to what extent the clinical guidelines were followed and to calculate the response time (time from CTG+ST guideline indications to delivery).

The CTG+ST clinical guidelines

CTG+ST clinical guidelines (Amer-Wählin *et al* 2007) provide detailed information on the definition of normal, intermediary, abnormal and preterminal FHR patterns (Table III). In case of an intermediary or abnormal CTG pattern, ST analysis was used as an adjunct to indicate when intervention is required (Table V). FBS was also used as an additional source of information both among CTG and STAN cases.

Classification of CTG

The intended use of this CTG classification system is to suggest clinical conditions in which adjunctive use of ST waveform changes may aid the interpretation of specific CTG patterns.

	Baseline heart frequency	Variability Reactivity	Decelerations
Normal CTG	<ul style="list-style-type: none"> • 110–150 bpm 	<ul style="list-style-type: none"> • Accelerations • 5–25 bpm 	<ul style="list-style-type: none"> • Early uniform decelerations • Uncomplicated variable decelerations with a duration of <60 sec and loss of <60 beats
Intermediary CTG	<ul style="list-style-type: none"> • 100–110 bpm • 150–170 bpm • Short bradycardia episode (<100 bpm for ≤3 min) <p>A combination of several intermediary observations will result in an abnormal CTG</p>	<ul style="list-style-type: none"> • >25 bpm (saltatory pattern) • <5 bpm >40 min with absence of accelerations 	<ul style="list-style-type: none"> • Uncomplicated variable decelerations with a duration <60 sec and loss of >60 beats
Abnormal CTG	<ul style="list-style-type: none"> • 150–170 bpm and reduced variability • >170 bpm • Persistent bradycardia (<100 bpm for >3 min) 	<ul style="list-style-type: none"> • <5 bpm for >60 min • Sinusoidal pattern 	<ul style="list-style-type: none"> • Complicated variable decelerations with a duration of >60 sec • Repeated late uniform decelerations
Preterminal CTG	<ul style="list-style-type: none"> • Total lack of variability (<2 bpm) and reactivity with or without decelerations or bradycardia 		

Table III. CTG+ST clinical guidelines, classification of CTG.

The recommendation for using ST analysis is to start the recording at least 30 minutes prior to onset of active pushing and to continue the recording until sufficient information has been obtained to expedite delivery. In case there are no indications to intervene, the recording should continue until delivery or at least within 20 minutes of delivery. In case of lack of ST data for more than four minutes, it is recommended that obstetric management be decided from the FHR information alone.

ST Analysis

These guidelines may indicate situations in which obstetric intervention¹ is required.

ST Events	Normal CTG	Intermediary CTG	Abnormal CTG	Pretermal CTG
Episodic T/QRS rise	<ul style="list-style-type: none"> • Expectant management • Continued observation 	• >0.15	• >0.10	<ul style="list-style-type: none"> • Immediate delivery
Baseline T/QRS rise		• >0.10	• >0.05	
Biphasic ST		• 3 Biphasic log messages ²	• 2 Biphasic log messages ²	

¹ Intervention may include delivery or maternal-fetal resuscitation by alleviation of contributing problems such as over-stimulation or maternal hypotension and hypoxia.

² The time span between the Biphasic messages should be related to the CTG pattern and the clinical situation.

Table IV.

CTG+ST clinical guidelines, ST analysis.

Education and training

During the studies, labour ward personnel were systematically instructed and trained in (patho-) physiology of asphyxia and CTG and ST interpretation using educational material (Sundström *et al* 2000) and review of their own cases.

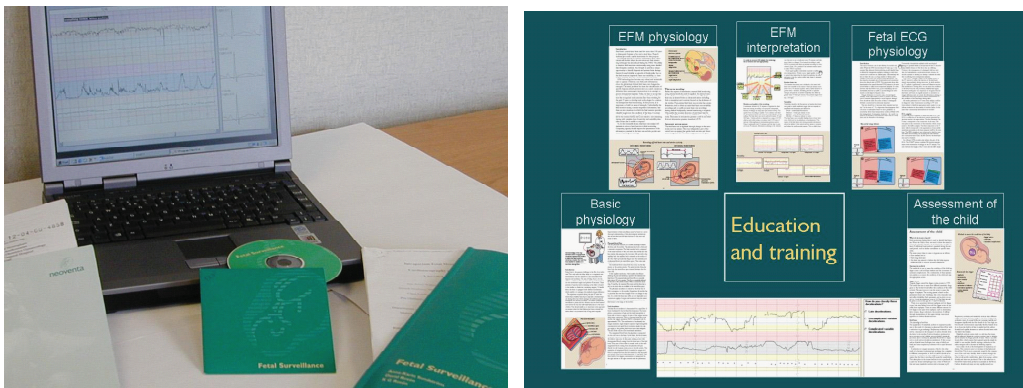


Figure 10. Education and training material used in the EU study

Each ward had a part time midwife responsible for the education and data collection according to a protocol used throughout the European Union multi-centre trial (**Papers I, III and IV**). Apart from the STAN recordings that were stored digitally, non-personalised clinical data was entered on a case record form, subsequently checked for consistency of data and entered into a standard database format.

According to the protocol, all patients that entered the study would have the umbilical cord artery and vein acid-base status assessed at delivery. Cord artery and vein samples were obtained routinely using immediate cord clamping and acid base data were checked for accuracy according to A-V pCO₂ difference of 1.0 kPa and pH \geq 0.03 Units. Metabolic acidosis was defined as cord artery pH <7.05 and BD_{ecf} >12.0 mmol/l. BD_{ecf} was calculated using the Siggaard-Andersen 'Acid Base Chart algorithm' (Siggaard-Andersen 1971).

In case of no cord acid-base data available, the case would still be counted for according to the criteria outlined in previous chapter 'Assessment of acid base data'.

Specific aspects

STAN in clinical practice – The outcome of 2 year regular use in the city of Göteborg (**Paper I**)

The two labour wards located at Sahlgrenska University Hospital, Östra and Mölndal cover a population of 870 000. The two wards were equipped with eight STAN units in August – September 2000 after the educational process had been ongoing during the summer months. An additional three STAN units were installed during the last six months of the study. The two units are large labour wards with approximately 4000 deliveries per year each and 300 members of staff. Continuous fetal monitoring (conventional EFM) is the norm during second stage of labour. One of the labour wards participated in the Swedish RCT (Amer-Wåhlin *et al* 2001).

The general indications for using ST analysis were 36 completed gestational weeks and situations where internal monitoring was the preferred method of fetal surveillance. Specific indication included high-risk pregnancies, women with suspicious or abnormal external CTG antenatally or in early labour, labour induction, oxytocin augmented labour and presence of meconium stained amniotic fluid. Additional use of ST analysis also became part of the training aspect.

Clinical records at the two neonatal units were reviewed for cases of moderate/severe neonatal encephalopathy (Low 1997) excluding cases with lethal malformations (one trisomia 13, two trisomia 18, two CNS malformations). Recordings originating from cases with adverse neonatal events or metabolic acidosis were reviewed and agreed upon by at least two of the authors. The assessment of tracings was performed without access to outcome data. Neonatal encephalopathy was defined as follows: minor, with irritability and jitteriness; moderate, with profound lethargy or abnormal tone; and severe, with coma or abnormal tone and seizures.

STAN, a clinical audit: the outcome of 2 years of regular use in the city of Varberg, Sweden (**Paper II**)

The delivery ward at Varberg Hospital is a middle sized obstetric unit with approximately 1800 deliveries per year. The staff consists of approximately 40

midwives and 20 physicians are involved in fetal monitoring during labour. ST analysis was introduced at the hospital in April 2002 when two STAN units were acquired. In 2005, one additional unit was installed. The current analysis investigated the perinatal outcome over a two year period between January 1st 2005 and December 31st 2006. Three midwives and two physicians were initially trained to become trainers of the rest of the staff. The training consisted of lectures, written information and multimedia based teaching. The ward had one physician and one midwife who were responsible for the continued education, data collection and case based discussions. The hospital does not have a neonatal care unit and risk pregnancies are referred elsewhere. This would include severe complications during pregnancy and/or intercurrent disease in mother and/or child when you could assume that the child needs neonatal care after delivery.

The general indications for using ST analysis were 36 completed gestational weeks and when a decision to use a scalp electrode for fetal surveillance was made. The specific indications for use of ST analysis were abnormal CTG pattern, meconium stained amniotic fluid, postmaturity, pre-eclampsia, diabetes, intra uterine growth retardation (IUGR) and twins. Because of the restricted number of STAN units, not all patients with CTG abnormalities could be monitored with CTG+ST analysis.

The CTG+ST clinical guidelines gave information on the definition of normal, intermediary, abnormal and preterminal CTG patterns. ST analysis was used when the CTG pattern was intermediary or abnormal. FBS was left at the discretion of the attending physician regardless of monitoring technique.

Fetal scalp pH and ST analysis of the fetal ECG as an adjunct to CTG. A multi-center, observational study (Paper III)

The study was undertaken as part of the European Union ST analysis trial, an EU supported multi-centre project on intrapartum fetal monitoring. It involved the following obstetric units: Sahlgrenska University Hospital Göteborg, University Hospital Turku, Rikshospitalet Oslo University, Gentofte Hospital University of Copenhagen, Virchow Klinikum Charité Berlin, Hospital Eduard Herriot University of Lyon, Derby City General Hospital University of Nottingham, University Hospital of Perugia, University Hospital Utrecht and Derriford Hospital University of Plymouth under the coordination of Neoventa Medical, Mölndal.

ST analysis monitoring was used in high-risk pregnancies, women with suspicious or abnormal external CTG, induced or oxytocin-enhanced labour or meconium-stained amniotic fluid. The decision to take FBS was left at the discretion of the clinician in charge and the time and pH reading was recorded. Cord artery metabolic acidosis was defined as a pH <7.05 in combination with a $BD_{\text{cef}} > 12.0$ mmol/l. Cord artery respiratory acidaemia was defined as cord artery pH <7.06 regardless of the BD_{cef}

Fetal scalp pH and ST analysis of the fetal ECG as an adjunct to CTG to predict fetal acidosis in labour (**Paper IV**)

This study is an extension of **Paper III** where additional cases of moderate acidaemia are added together with a control group.

The marked acidosis group included all cases with cord artery pH <7.06 (53 cases) and the moderate acidaemia group consisted of cord artery pH ranging from 7.06 – 7.09 (44 cases). Corresponding controls were identified from the database as the case recorded as the previous or next case, depending on which one was the closest, at the same site as the acidaemic case with a cord artery pH \geq 7.20.

Statistical analysis

The results were statistically evaluated with the Medcalc[®] statistical software (version 5, Medcalc, Mariakerke, Belgium). Student's t-test or Mann-Whitney's test was used for testing statistical significance for continuous variables. χ^2 or Fisher's exact tests was used for discrete variables and the odds ratios (OR) with 95% confidence intervals (CI) was calculated. P-values < 0.05 were considered significant.

General study design

In the European Union ST analysis trial, the overriding project was aimed at investigating a method of dissemination of knowledge whereby academic units across Europe became regional Centres of Excellence (CoE). These CoEs would then provide quality assurance regarding ST analysis for education, training and certification. The initial task among these centres was to validate their own outcome and performance with the new methodology.

Paper I constitutes the outcome over two years in the labour wards covering the total population of term deliveries in active labour in the city of Göteborg. These data represent the outcome from one of the CoE. The validation was subsequently extended to a district hospital audit covering two years of CTG+ST usage at the Varberg hospital (**Paper II**).

ST analysis of the FECG is intended as an adjunct to standard CTG interpretation. FBS with scalp pH analysis has served as an objective marker of intrapartum hypoxia. As part of the European Union trial, a large database was generated including close to 8000 digitalized EFM recordings with continuous FECG analysis, detailed notes on clinical performance and neonatal outcome. From these data the hypothesis that CTG+ST changes are as accurate as CTG+FBS data in detecting intrapartum hypoxia and acidaemia were tested. For this purpose, cases requiring FBS due to abnormal FHR and subsequently cord artery acidaemia at birth were identified and analysed. The aim of the study (**Paper III**) was to test the hypothesis that CTG+ST clinical guidelines identify cases of intrapartum acidosis with accuracy similar to that of CTG+FBS.

With the opportunity of improving standards of intrapartum care, detailed information on different patterns of events is required. Thus, the analysis of the ST+FBS cohort of 911 cases was extended with the aim to analyse the sequence of CTG, FBS and ST changes as part of a case control study of cord artery acidosis (**Paper IV**).

Results and Comments

Papers I and II

CTG+ST usage rates

In the city of Göteborg (**Paper I**) during the two year period between October 1st 2000 and September 30th 2002, 14687 deliveries entered active labour with a gestational age of more than 36 completed weeks. Of these, 4830 (32.9%) were monitored with CTG+ST analysis and a significant increase in usage was noted comparing year one to year two (28% versus 38%, $p<0.001$). For comparison, the CTG+ST usage rate in the Varberg audit was 59% after two years. Although there were clinical indications for the use of ST analysis, the majority of cases had ST analysis undertaken on the basis of midwives decision and the need for more accurate information.

Interventions for fetal distress

Table V provides a summary of operative intervention rates in **Paper I and II**.

			Total operative deliveries for fetal distress (ODFD)			CS for fetal distress			VE/Forceps for fetal distress		
City of Göteborg study											
Year	No of cases	Monitored CTG+ST	CTG+ ST ^a	CTG	Total	CTG+ ST ^a	CTG	Total	CTG+ ST ^a	CTG	Total
1	7325	2057 (28.1%)	11.1%	4.8%	6.6%	5.2%	2.5%	3.2%	5.9%	2.3%	3.3%
2	7362	2773 (37.7%)	10.3%	3.6%*	6.1%	5.1%	1.9%	3.1%	5.2%	1.7%	3.0%
Varberg audit											
2 years	3193	1871 (59%)	6.8%	6.7%	6.7%	3.1%	4.2%	3.5%	3.7%	2.5%	3.2%

Table V. Operative delivery rates. ^a Cases with perceived risk and need for close surveillance with CTG + ST available. * = $p<0.05$

Both cohorts cover all women in active labour at term. The total ODFD rates were the same in the different populations. Although, the group monitored with

conventional CTG should be at low risk with less operative deliveries as found in the Göteborg data, in Varberg the total CS rate was significantly reduced in the CTG+ST group. Among the acute CS for ODFD in Varberg, emergency (crash) CS were also significantly reduced from 1.51% (19 cases) to 0.27% (5 cases) in the CTG and CTG+ST monitored groups respectively (OR 0.18, 95% CI 0.07-0.49). Of the five crash CS cases monitored with CTG+ST, four had CTG+ST indications to intervene. None of the 24 cases had metabolic acidosis and only one had Apgar below seven at five minutes (CTG monitored case). Thus, it appears that lack of continuous information about fetal myocardial reaction causes increased uncertainty in the timing of intervention resulting in more emergency procedures. The rates of operative deliveries for reasons not including fetal distress were 8.0% (year 1) and 8.6% (year 2), the corresponding figure for the Varberg audit was 9.0%.

In fetal monitoring, it is important not only to decide when to intervene but also to avoid an intervention when not indicated. Apart from analysing the rate of interventions, the relationship between indications to intervene, mode of intervention and outcome were assessed. Table VI gives the details from the Varberg audit when a decision to intervene operatively for fetal distress was made. The extent to which the clinical guidelines had indicated a need to intervene was made retrospectively and without knowledge of outcome.

Operative deliveries for fetal distress	Number of cases / % of all deliveries	Cord artery pH (mean, 95% CI)	Comments
CS for fetal distress			
According to CTG+ST guidelines	32/1.8	7.19 (7.14-7.23)	
Outside CTG+ST guidelines	26/1.3	7.26** (7.23-7.28)	3 cases had a normal CTG and ST events, 2 cases had normal CTG+ST and 21 cases had CTG changes with normal ST. Lowest cord art pH 7.12, all had Apgar \geq 7 at 5'
Vag op deliv for fetal distress			
According to CTG+ST guidelines	41/2.2	7.14 (7.11-7.17)	
Outside CTG+ST guidelines	28/1.5	7.19* (7.16-7.22)	2 cases had normal CTG+ST, 26 cases had CTG changes with normal ST. All cases had Apgar 9-10 at 5', 4 cases had respiratory acidaemia (pH 7.06 – 7.09).

Table VI. ODFD according to/and outside CTG+ST clinical guidelines from Varberg database. * = $p < 0.05$. ** = $p < 0.01$, unpaired T-test

Cord artery pH data show significant differences related to the extent to which the CTG+ST clinical guidelines were followed or not. Those cases delivered with CS for fetal distress outside the guidelines had the same cord artery pH as those delivered by CS for FTP (pH 7.27; 7.25-7.29, p=0.50). The same observation was made with regard to vaginal operative deliveries with FTP cases showing cord artery pH 7.19; (7.17 – 7.21, p=0.92). It may also be noted that of the 58 cases with CS, five were intervened upon despite a normal CTG according to the retrospective analysis. In three of these, ST events were recorded in connection with the intervention, corresponding to 0.16% of those monitored with ST analysis.

Of all ODFD (127 cases), 47 cases (21 CS and 26 VE), corresponding to 2.5% of all deliveries, had an operative intervention outside of the guidelines because the CTG pattern was considered abnormal to the extent that an operative delivery was perceived to be required. This is most likely the outcome measure that will be the most markedly affected by increasing user experience and trust in the new method. In a recently conducted US study of initial exposure to ST analysis the corresponding figure was significantly higher 5.3% (28/530) (OR 0.46; 95% CI 0.27-0.75) (Devoe *et al* 2006),

Validated cord artery metabolic acidosis

The increased use of ST analysis in the ‘City of Göteborg’ (GOT) study was associated with a significant reduction in cord artery metabolic acidosis rates in the group monitored with CTG+ST as well as in the total population, OR and 95% CI; 0.49, 0.25-0.98 and 0.58, 0.37-0.93, respectively. No further improvement in metabolic acidosis rate was noted as ST analysis usage increased from 38% (GOT second year) to 59% (Varberg).

	Cases with cord acid base data		Cord artery metabolic acidosis rates		
	CTG+ST ^a	CTG	CTG+ST ^a	CTG	Total
GOT study					
Year 1	1868/2057 90.8%	4721/5268 89.6%	21/1868 1.12%	29/4721 0.61%	50/6589 0.76%
Year 2	2503/2773 90.3%	4083/4589 89.0%	14/2503 0.56%*	15/4083 0.37%	29/6586 0.44%*
Varberg audit					
2 years	1776/1871 94.9%	1222/1322 92.4%	8/1776 0.45%	7/1222 0.57%	15/2998 0.50%

Table VII. Fetal outcome. ^a Cases with perceived risk and need for close surveillance. *= p<0.05.

CTG+ST clinical guidelines include recommendations on the response time. During the first year there were 21 cases born in Göteborg with cord artery metabolic acidosis. Out of these, 14 had ST events recorded in combination with CTG changes

and occurring more than 17 minutes before delivery in second stage and more than 25 minutes in first stage of labour indicating a prolonged response time. This gives an incidence of 0.75% (14/1868) of cases with a prolonged response time.

During the second year, 14 metabolic acidosis cases were recorded. The number of cases with a prolonged response time was significantly reduced during the second year to 0.28% (7/2503), (OR 0.37, 0.15-0.92). The corresponding rate of cases with a prolonged response time in Varberg was 0.17% (3/1776).

A summary of CTG and ST changes, mode of delivery and neonatal outcome is given in Table VIII. Of the 41 cord artery metabolic acidosis cases with CTG+ST data available, ten did not present abnormalities according to CTG+ST clinical guidelines, eight of these showed intermediary/normal CTG patterns and all ten cases had uncomplicated neonatal periods.

	CTG pattern		Significant ST events			Mode of delivery		Neonatal course	
	Abnormal 1 st stage / preterminal	Abnormal 2 nd stage	Inter-medialy/ normal	Baseline T/ QRS rise	Biphasic ST	ODFD	Normal vaginal, delivery	Uneventful	Complicated
GOT ^a , 4371 cases	5/2	19	8/0	25	1	14	21	30	5 ^b
Varberg ^c , 1776 cases	1/1	4	1/1	4	-	3	5	4	4 ^d

Table VIII. Summary of CTG and ST changes, mode of delivery and neonatal outcome. a - 35 cases, one case had STAN disconnected for 1h 16 min prior to delivery and EFM data could not be assessed, and one case with no ST data last 28 min. b - Complications included sepsis (1 case), meconium aspiration/respiratory distress (2 cases), HIE, gr II (2 cases). c - Eight cases, all with CTG+ST data available but one case starting during second stage and not following CTG+ST clinical guidelines. d - Two cases with meconium aspiration and two cases with HIE, gr II and III.

These data indicate that a CTG+ST guidelines indication to intervene occurred in 83% (33/40) of the cases where CTG+ST data was available and the recording started according to recommendation prior to active pushing, i.e. adequately recorded cases. The dominant fetal pattern of reaction in connection with metabolic acidosis was an ST rise occurring in connection with an abnormal CTG pattern during second stage. It may also be noted that 78% of the cases with cord artery metabolic acidosis had an uneventful neonatal course.

Moderate and severe neonatal encephalopathy monitored by CTG+ST

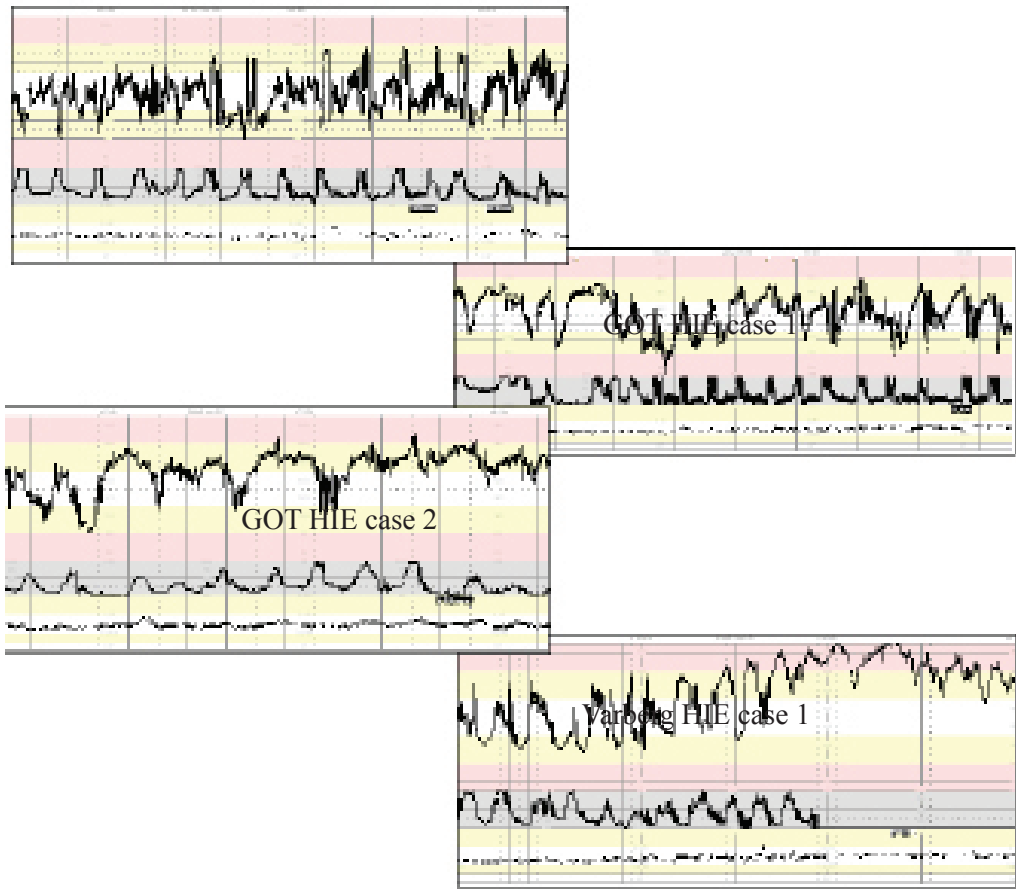
Table IX provides a summary of all cases with HIE diagnosis defined as acidosis at time of delivery, low Apgar scores at five minutes, need for resuscitation and abnormal neurological findings.

Case	CTG pattern	pH art	pCO ₂ art kPa	BD _{ref} art	FBS pH	ST event	Time ST event to birth (min)	Mode of delivery	AS 1/5	Perinatal outcome
GOT 1	Abn 2nd stage	6.97	6.69	18.0	-	Base-line rise 0.11	79	SVD	3/5	Mec aspir. seizures at 12h. abn EEG. multi organ symptoms. 20d in NICU. HIE gr II
GOT 2	Abn 2nd stage	6.94	9.3	15.3	-	Base-line rise 0.06	44	SVD	4/5	Normal cardiopulm adaptation. hypertonus and seizures during 24h. abn EEG. normal CT. HIE II
V-berg 1	Abn 1st stage	-	-	-	7.23 and 7.17	Base-line rise 0.06	46	Complicated C/S	0/0	Multiorgan symptoms, HIE III, parasagittal infarcts on MRI
V-berg 2	Abn 2nd stage	7.01	8.75	12.9		Base-line rise 0.06	27	Complicated VE	3/5	HIE II, parasagittal bleedings + capsula interna ischaemia on MRI

Table IX. Summary of all HIE cases in **Paper I and II**.

The overall incidence of HIE gr II and III was 0.65 % (4/6147). Although the cases are few, relevant information may still be obtained by analyzing the reason for the delay in delivering these fetuses and the CTG pattern in particular associated with the ST events. Figure 11 provides a snapshot of the part of the tracings where the initial significant ST event occurred. From these data it appears as if the dominant pattern associated with an ST rise was unstable FHR with marked variations, including beat-to-beat.

Such patterns may previously have been regarded as erroneous due to miss triggering but this is no longer the case with the availability of modern digital signal processing.



Varberg HIE case 2

Figure 11. Samples of CTG+ST sequences obtained at time of ST event in the four cases with HIE grade II and III

Summary of the clinical outcome data

It can always be argued that a clinical trial provides special focus on the issues studied. Thus, it should be interesting to further document the introduction of a new technology as was done with the current study originating from busy labour wards with a large number of caregivers.

Paper I contained a population based prospective study covering the total number of deliveries in the city of Göteborg, over two years. During the second year of the study period, metabolic acidosis rates were below what was seen in the CTG+ST group of the Swedish RCT (Amer-Wählin *et al* 2001), 0.56% and 0.69% respectively. The rate noted in the CTG+ST group during the second year was similar to that

recorded after retraining in the Swedish RCT (0.52%).

The reduction in cases with cord artery metabolic acidosis noted within the two years could be related to two major findings: (1) the increase in use of ST analysis and (2) the improved response time to ST events associated with significant CTG changes.

The response time is dependent on the ability of the staff to assess the data in a uniform fashion. The hypothesis that the addition of ST analysis to standard FHR tracing analysis would improve the consistency and accuracy of clinical decision making has been tested by Ross *et al* 2004. Using the outcome of observer agreement for need and timing of intervention, experienced users showed more consistent and accurate assessment of data as ST analysis was added as compared to standard FHR analysis.

The implication of the findings of the Swedish RCT (Amer-Wählin *et al* 2001) was that the majority of cases with an adverse outcome of labour had no antenatally known risk factor. Thus CTG+ST should have a role to play also in a low risk environment such as in a general district hospital. The Varberg audit (**Paper II**) provides data which are coherent with what was noted in both the CTG+ST arm of the Swedish RCT and the 'City of Göteborg' study second year outcome

Papers III and IV

ST analysis and FBS as adjuncts to CTG

ST analysis serves as an adjunct to standard CTG similar to what has been the case with FBS. The issue evaluated in these studies is to what extent these two additional parameters complement each other.

In the large European Union ST analysis trial database of 7823 deliveries, 6999 deliveries were recorded in centres using FBS (**Paper III**). FBS was performed in 13% (911/6999) of the cases. In 53 cases, marked cord artery acidosis (pH <7.06) was found and 44 cases showed moderate cord artery acidaemia (pH 7.06-7.09) at birth. Comparisons were made with 97 control cases (pH \geq 7.20) (**Paper IV**). Apart from one perinatal death (e-coli septicaemia) no adverse neurological findings were noted during the neonatal period among the 194 cases. Table I provides baseline characteristics of the different groups.

SCBU admission was associated with low Apgar scores (<7 at 5 minutes) in 15 of the 26 cases (58%) with marked acidaemia and four of the 14 (26%) cases with moderate acidaemia. The corresponding rate for the control groups was one out of 12 (8%). No relationship between antenatal risk factors and degree of cord acidaemia and acidosis could be noted.

Indications to intervene

Metabolic acidosis group

Of the 20 cases with metabolic acidosis, 19 had adequate ST analysis information. One case with adequate data of the total group of 20 cases was not identified by CTG+ST giving a sensitivity of 95%. Figure 12 shows the STAN recording of this case. All five fetuses with Apgar scores below six at five minutes were identified by CTG+ST changes. All 12 cases with FBS data obtained within one hour of delivery and in connection with metabolic acidosis showed acidaemia with the highest pH of 7.16, giving a sensitivity of 100%. Kappa statistics for comparisons between pH <7.15 obtained within the last hour of labour and ST events showed a Kappa value of 0.63, indicating a moderate level of agreement (Sim and Wright 2005).

	Antenat risk factors, %	Primi gravidae %	ODFD %	Apgar scores median		Cord artery, median		BD _{ecf} mmol/l	SCBU
				1'	5'	pH	pCO ₂ kPa		
Marked acidosis group, n = 53	26	75	66***	5***	8***	7.01	9.80	11.1	49%***
Control group 1, n = 53	26	74	28	9	10	7.25	6.61	4.1	15%
Moderate acidaemia group, n= 44	16	77	55***	7***	9***	7.08	9.04	9.11	32%*
Control group 2, n = 44	18	70	18	9	10	7.25	6.75	3.4	11%

Table X. Baseline characteristics of the groups. Antenatal risk factors included: >42 gestational weeks, oligohydramnios, pre-eclampsia, hypertension, diabetes mellitus, premature rupture of membranes and growth retardation. ***, $p < 0.001$, unpaired t-test or Chi².

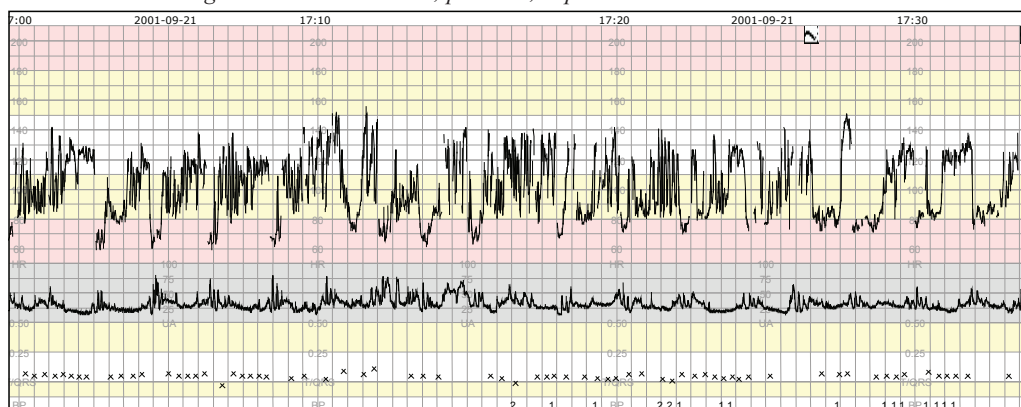


Figure 12. STAN recording obtained during second stage of labour ending eight minutes before the baby was delivered by an outlet VE. FBS pH 7.16 obtained at onset of recording. Apgar scores 7-9-10 at 1, 5 and 10 minutes. Cord artery pH 7.03, pCO₂ 8.53 kPa, BD_{ecf} 12.3 mmol/l, normal neonatal period.

	Total no of cases/ no of SCBU admis- sions	Intervention according to CTG+ST guidelines; no of cases; median and range of time between indication to intervene and delivery, minutes	Intervention according to FBS <7.20; no of cases, median scalp pH and range
Cord metabolic acido- sis and Apgar scores <6 at 5'	5/5	5 cases 34 (26–103) minutes	4 cases pH 6.97 (6.92–7.14)
Cord metabolic acido- sis and Apgar scores >5 at 5'	15/10	13 cases 25 (2–46) minutes	8 cases pH 7.07 (6.94-7.16)

Table XI. Summary of the data available in the metabolic acidosis group.

One aspect to consider is the lag time between indications to intervene, according to CTG+ST guidelines, and delivery in the metabolic acidosis cases and the potential delay in case FBS was obtained. Among the 20 cases with metabolic acidosis, eleven had FBS obtained after the guidelines had identified abnormality. In eight of these cases a progressive rise in T/QRS baseline occurred. Figure 13 gives the relationship between the lag time (time between last ST event and FBS) and scalp pH in these eight cases.

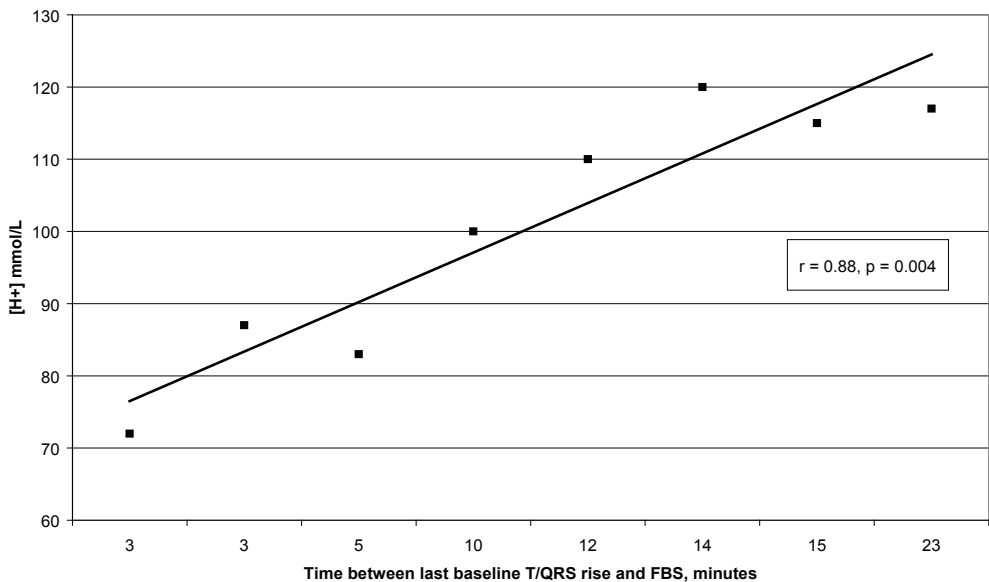


Figure 13. A plot of the relationship between the number of minutes that elapsed from a ST event of a baseline T/QRS rise to FBS and the calculated hydrogen ion concentration $[H^+]$. The linear regression line is included together with the corresponding correlation coefficient and p-value.

The delay issue in responding to information can be illustrated by the finding that of the 15 cases with metabolic acidosis requiring SCBU, all 14 cases adequately monitored on CTG+ST had indications to intervene for 19 minutes or more prior to delivery. Figure 14 illustrates such a case of progressive T/QRS rise in second stage of labour where the FHR pattern may not look that ominous. FBS was obtained at 04:22 (pH 7.06) and an operative vaginal delivery occurred 20 minutes later giving a lag time from the ST event indication to intervene to delivery of 36 minutes. Similar FHR patterns was seen in the above described HIE cases.

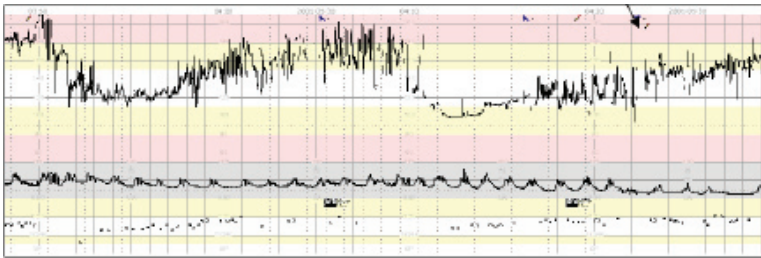


Figure 14. Recording obtained during second stage of labour in a para 0 with pre-eclampsia, outlet VE delivery at 04:42, Apgar scores 2-7-8, cord artery pH 6.97, $p\text{CO}_2$ 8.40 kPa, BD_{ect} 15.3 mmol/l. An FBS was obtained at 04:22 (arrow), pH 7.06. The baby was admitted to SCBU, recovered initially but collapsed at 2h and died from e-coli septicaemia.

Of the 53 cases with marked cord acidosis, 22 cases had an FBS obtained after the ST event thus adding to the response time. The median time between the significant ST event and FBS was 14 minutes (range 8-25, 95th CI). One of these cases is illustrated in Figure 15.

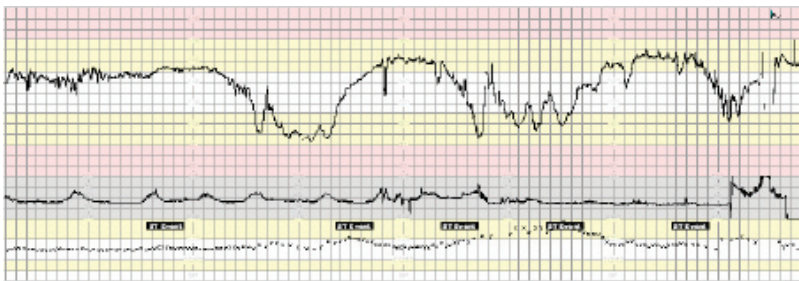


Figure 15. Para 1, spontaneous onset of delivery after 39 weeks. Indications to intervene at 11:59. Two FBS (pH 6.92 and 6.93) at 12:20 and 12:22. CS for fetal distress at 12:39. Apgar 1 at 1min. ,4 at 5 min., cord art pH 6.93, BD_{ect} 12.4 mmol/l. Uneventful observation in special care.

Identification of acidosis and non-acidosis situations

The extent to which adverse situations will have an impact of cord artery pH is a function of time. Figure 16 shows the distribution of cases in relation to time between the CTG+ST indications to intervene and time of delivery. The graph indicates the proportion of cases within a certain acidosis/control group that start showing CTG+ST abnormality in relation to time to delivery. In the control group, 57% (17/30) of the events occurred within 16 minutes of delivery as compared to 16% (11/67) in the combined acidosis group (OR 6.66, 2.29 – 19.86, $p < 0.001$). Of the remaining 13 cases (43%) in the control group, two cases displayed biphasic ST (followed by normal FBS), two showed persistent CTG+ST changes (one normal FBS) and nine had episodes of decelerations plus increased T/QRS ratio in first stage of labour, emerging more than one hour prior to delivery in seven cases. Among the nine cases, two had abnormal FBS, pH 7.09 and 7.14 obtained within ten and 12 minutes of the CTG+ST event respectively.

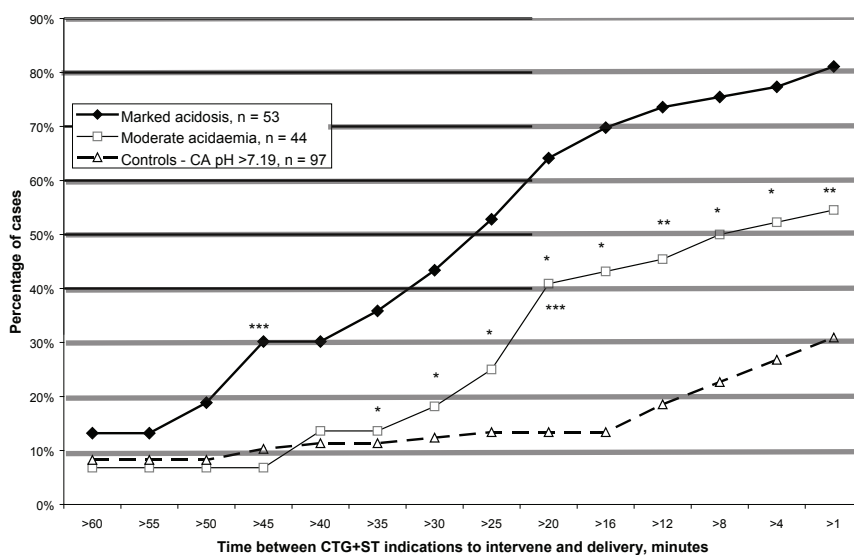


Figure 16. The figure illustrates the occurrence of CTG+ST clinical guideline indications of need to intervene in relation to minutes remaining until delivery. Cases are grouped according to level of cord artery pH (marked acidosis; $pH < 7.06$, moderate acidaemia; $pH 7.06 - 7.09$, controls; $pH \geq 7.20$.) CTG+ST changes are significantly more frequent as compared to controls 45 minutes (marked acidosis) and 20 minutes (moderate acidaemia) before delivery (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, χ^2 -test).

The time factor, i.e. the time between onset of significant ST events and delivery can be illustrated by the observation that of those with CTG+ST events recorded within 16 minutes of delivery, 61% had cord artery $pH \geq 7.20$. The corresponding figure for cases where CTG+ST indications occurred more than 16 minutes before delivery was 19% (OR 6.66, 2.29 – 19.86, $p < 0.001$). Thus, the most common scenario would be the onset of myocardial anaerobic metabolism, as identified by an increase

in T/QRS, occurring at a fetal pH of >7.20 . This observation is supported by pH <7.20 occurring on average 14 minutes after a significant CTG+ST event in cases with marked acidosis. The corresponding figure in cases with CTG changes at start of a ST analysis recording was 29 minutes (**Paper IV**).

Abnormal FHR, ST analysis and FBS

Out of the 194 cases included in the study, 121 had abnormal CTG patterns, 94% (50/53); 77% (34/44) and 38% (37/97) of the cases were obtained from marked acidosis, moderate acidaemia and controls, respectively.

Of the 121 cases with an abnormal CTG, 84 (69%) showed a cord artery pH of <7.10 . ST waveform changes indicated a need for intervention in 83% (70/84) of these. Of the seven cases with abnormal FBS and normal CTG+ST, six had respiratory acidosis with normal neonatal period and one case had normal cord artery pH (≥ 7.20). All these seven cases had the low scalp pH obtained during second stage.

Of the 12 cases with abnormal CTG+ST changes but normal FBS, five developed acidosis subsequently and seven had a normal cord acid base.

Comments

Although ST and scalp pH are equally capable in identifying cases with intrapartum asphyxia (metabolic acidosis and low Apgar), with ST changes emerging on average 14 minutes prior to an abnormal scalp pH, some discrepancy is noted in cases of respiratory acidaemia developing in second stage of labour. Obviously, the significance of identifying those cases can be discussed. More relevant is what information is obtained in first stage when CTG is indicating abnormality and ST+FBS is normal. In such situations continuous information is essential in case of perinatal asphyxia developing. The patterns recorded among the 61 cases that showed CTG changes at onset were examined to analyse if FBS added value in those cases

Cases with CTG changes at start of ST analysis

Table XII summarises the relationship between ST findings recorded prior to FBS in cases with CTG changes at onset.

CTG+ST guidelines indicated abnormality prior to an abnormal FBS in 14 out of 17 cases. In all of these cases CTG changes were noted already at onset of the recording. The median duration between CTG+ST indications to intervene and an abnormal FBS was 29 minutes (range 11-74, 95% CI). Of the three cases not identified by CTG+ST, two had a late onset of the recording in second stage and the third had an FBS obtained nine minutes before a spontaneous vaginal delivery in connection with bradycardia and uterine rupture (cord artery pH 6.97, $p\text{CO}_2$ 15.0 kPa, BD_{ecf} 5.0 mmol/l, normal neonatal period).

Furthermore, of those 14 cases in the marked acidosis group that showed a normal ST+FBS initially, 11 (79%) subsequently developed ST changes and those that did not show ST changes had their recordings disconnected for more than 25 minutes prior to delivery. In the moderate acidosis group only two cases showed ST changes

after an initially normal ST+FBS sequence.

The data does not support the need for an FBS in case of CTG changes at onset of the CTG+ST recording. However, as previously stated, if there is evidence of an unstable fetal condition, an FBS is required in case a decision is made to continue labour. The alternative is to decide to intervene and deliver based on the fact that there is sufficient information to identify inadequate fetal response and inability to maintain steady-state.

Intervention caused by overreacting to CTG or CTG+ST data may constitute a problem. Although, the RCTs (Westgate *et al* 1993, Amer-Wåhlin *et al* 2001) showed fewer interventions for fetal distress with CTG+ST, this may be an issue worthy some further documentation. The Varberg audit (**Paper II**) provided an opportunity to study the clinical application of CTG+ST clinical guidelines. From these data (Table VI) it appeared that when action was done on the basis of an intermediary/abnormal CTG pattern only, the cord-acid base was identical to the situation where intervention was done for FTP. One other aspect to consider is the extent to which an ST event may cause an intervention despite a normal CTG. Of the 58 cases with CS in the Varberg study, five were intervened upon despite a normal CTG in the retrospective analysis. In three of these, ST events were recorded in connection with the intervention, corresponding to 0.16% of those monitored with CTG+ST.

Cases with CTG changes at onset – 61/194 cases	Normal FBS		Abnormal FBS	
	Normal CTG+ST	Abnormal CTG+ST	Normal CTG+ST	Abnormal CTG+ST
Marked Acidosis group, n = 21/53	14	0	2 (One inadequate recording started in 2 nd stage and one case had a uterine rupture in connection with a normal vaginal delivery)	5
Moderate Acidaemia group, n = 16/44	6	1	1 (Inadequate recording started in 2 nd stage)	8
Controls, n = 24/97	23	0	0	1
Total	43	1	3	14

Table XII. Relationship between FBS and CTG+ST guideline indications of abnormality in cases with CTG changes (intermediary or abnormal) noted at start of ST analysis.

General discussion

The expectation of society is that the application of the results of health technology assessment should improve quality of care and to ensure that available resources are used effectively. The aim of the European Union ST analysis trial was to develop and validate a model whereby the user aspects are put to the fore to stimulate postgraduate training and an appropriate management structure. The data from this trial, presented as part of this thesis, has provided detailed information on the outcome when ST analysis was introduced clinically as an adjunct to standard CTG for fetal surveillance in term pregnancies.

Quality improvement research

The introduction of a new medical methodology requires RCTs to provide efficiency data comparing conventional methodology with the new. Apart from RCTs, quality improvement (QI) research may also be undertaken. QI is intended to result in improvements in care for an entire population of patients. Unlike RCTs, QI does not assign patients to different therapies or care practices, or require the testing of a hypothesis. Nevertheless, when QI is employed in a prospective manner, it can become as powerful as RCTs, and can be generalized to a similar extent (Ringer 2008).

Metabolic acidosis and HIE

The first aim of the present thesis was to demonstrate that the outcome of the Swedish RCT (Amer-Wählin *et al* 2001) could be verified in clinical praxis. In a cohort of 17880 term deliveries in active labour (**Papers I and II**), it was shown that the metabolic acidosis rate after the first year of CTG+ST usage was 0.51%. This is identical to the rate noted among CTG+ST cases in the Swedish RCT during the second phase of the study, when the staff had become accustomed to the new method.

This ability to maintain a low risk of metabolic acidosis also had an impact on the total metabolic acidosis rate (0.46%). The overall incidence of HIE gr II and III was 0.65 ‰ (4/6147). The four cases all showed a delay in responding (27, 44, 79 minutes in second stage and 46 minutes in first stage, respectively) adding to the significance of the CTG+ST method despite the rarity of significant HIE. Although these are rare cases, they are in focus when assessing fetal surveillance methods. There is now conclusive evidence that CTG+ST clinical guidelines will significantly decrease the risk of neonatal encephalopathy (RR 0.33; 95% CI 0.11-0.95) (Neilson 2006).

The FDA required American data before accepting the European research and experience (FDA 2005). This allowed for the new ST analysis method to be validated further and data was presented on the continuity of assessing CTG+ST information

both at bed-side and by experts (Devoe *et al* 2006).

The European Union trial involved ten academic centres across Europe some of which has published their own reports on CTG+ST. The Utrecht group was the first to summarise their findings (Kwee *et al* 2004), with 449 recordings available for analysis of outcome in relation to ST changes. Eighteen (4.0%) neonates were born with metabolic acidosis. Significant ST changes (18-31 min before birth) were present in all five cases with pH>7.00. The report concluded that CTG+ST analysis was more specific in detecting fetal acidaemia than CTG alone. One may comment that the high metabolic acidosis rate may partly be due to late cord clamping with falsely low pCO₂ reading.

More recently, the group from Lyon presented their data (Massoud *et al* 2007) from 1889 CTG+ST recordings. The metabolic acidosis rate was 0.38% with no adverse outcome and no false negative CTG+ST cases among the seven with metabolic acidosis. Their data also showed that over time with training and experience the adherence to the guidelines improved significantly as did the accuracy of the interpretation of the FHR.

The importance of meeting with the basic requirements of CTG assessment was highlighted in the report from St George's Hospital, UK (Doria *et al* 2007). Their data are rather disappointing in that no improvement was noted among the 1500 first cases monitored with CTG+ST. However, the reason identified by retrospective case based analysis was that CTG+ST guidelines were not followed and acted upon. The study identified the need for more intensive training and assessment of the users regarding the use of the CTG+ST analysis. Perhaps the outcome is a reflection of the British Royal College of Obstetrics and Gynaecology recommendation to use intrapartum EFM only in defined high-risk situations (RCOG 2001).

FBS and ST analysis as adjunct information to the CTG

Fetal surveillance is all about identifying when there is a risk of a fetus to be exposed to hypoxic stress beyond its capacity to respond. Basically, the FHR tracing depends on numerous factors. As a consequence, additional information is required to pin-point the situation when the fetus is no longer able to fully compensate.

The physiology of acidosis and ST events

A T/QRS rise in the FECG reflects myocardial anaerobic metabolism whereas a lowered pH in the blood (scalp-pH or cord blood pH) is largely a function of the free hydrogen ions (H⁺) generated by the accumulation of CO₂ (Figure 2) and the respiratory component of fetal acidosis will always dominate. This means that ST events may occur at a wide range of pH values but the more pronounced the drop in pH is, the more likely it is that it also contains a metabolic component. However, there will be situations where the pH may drop even below 7.0 without the myocardial anaerobic metabolism contributing to the accumulation of free hydrogen ions. Obviously, these are rare situations that need to be recognised by adequate cord acid base analysis and the calculation of BD_{ecf}. However, the common pattern is for

ST events to occur when pH has dropped below 7.20 and before it reaches 7.10.

As shown in **Paper II**, on average, the cord artery pH will drop to 7.19 (95th CI 7.14-7.23) when a CS is undertaken because of CTG+ST indications. In case of intermediary/abnormal CTG but no ST changes the corresponding pH is 7.26 (7.23-7.28). Thus the addition of an ST event will indicate a drop in cord artery pH by 0.07 units, and it may be speculated that this drop could be caused by the contribution of anaerobic metabolism. Furthermore, the CTG+ST events occurred prior to the cord blood being available and one would therefore assume a somewhat higher pH at onset of ST changes.

FBS has been the point of reference ever since CTG was introduced, although the effectiveness of the method in clinical practice has been questioned. In the Plymouth RCT (Westgate *et al* 1993), despite the use of a strict protocol, 39% of cases had FBS performed unnecessarily, and 33% of cases did not have it performed when it was indicated. The decision to obtain an FBS depends on the interpretation of the CTG. If the level of CTG interpretation is suboptimal, the value by monitoring with FBS is limited (Greene *et al* 1999).

In the Swedish RCT (Amer-Wählin *et al* 2001) the use of FBS in the two arms was 10.7% and 9.3%, respectively. In a trial from Dublin (Impey *et al* 2003) it was shown that as a result of admission test the use of continuous CTG and FBS increased (CTG from 42% to 58%, FBS from 8% to 11%) without signs of improved neonatal outcome.

In summary, FBS can be used along with CTG monitoring to assess fetal acid-base status during labour and can reduce operative intervention but it requires additional expertise, is time consuming and gives only intermittent information (Whebble *et al* 1989).

ST analysis and FBS – availability of information

Scalp lactate has recently been introduced as an option to more easily obtain a biochemical marker of ongoing hypoxia (Kruger *et al* 1999, Wiberg-Itzel *et al* 2008). In a recently published multi-centre RCT from Sweden, lactate and pH as adjunct to CTG were compared (Wiberg-Itzel *et al* 2008). It was not demonstrated that lactate was superior to pH, considering outcome markers such as ODFD or cord metabolic acidosis, although the success rate in lactate sampling was higher.

In the Swedish RCT on ST analysis as an adjunct to CTG (Amer-Wählin *et al* 2001) there was a significant reduction in metabolic acidosis and ODFD in the CTG+ST group. The question is how these parameters, FBS and ST serving as adjuncts to the CTG, interrelate.

Data from the Plymouth RCT (Westgate *et al* 1993) showed that it may be difficult to use FBS correctly. In the Swedish RCT (Amer-Wählin *et al* 2001), 496 cases out of 4966 monitored with both CTG and CTG+ST had a FBS. In the retrospective analysis, the ST information was made available also in the group monitored with CTG only.

The purpose of the FBS that were performed was to identify hypoxia and acidosis.

However, of the total number of metabolic acidosis cases in the trial (46 cases) FBS was obtained in only six cases. Of these six, five cases had CTG+ST indications to intervene and one case had no ST data available for retrospective analysis. FBS results were abnormal in only one case (pH 7.13).

The difficulty to use FBS correctly also emerged in the European Community (Luzietti *et al* 1999) and the Nordic observational study (Amer-Wählin *et al* 2002). In these studies of 894 (320+574) cases, FBS was performed in 78 cases (8.7%). In the cases with FBS, the CTG pattern appeared normal in 47%, intermediary in 31% and abnormal in 22%. Of the 78 cases, only six had a scalp pH <7.20. All of these cases had ongoing ST changes.

In the European Union trial database (**Paper III**) 20 cases had metabolic acidosis, 19 with adequate CTG+ST information and 11 had an FBS obtained after CTG+ST guidelines had identified abnormality.

Another important observation was that of those 14 cases (**Paper IV**) in the marked acidosis group (cord artery pH <7.06) that showed a normal CTG+ST and a normal FBS, 11 (79%) subsequently developed ST changes and those that did not show ST changes had their recordings disconnected for more than 25 minutes prior to delivery. Thus, continuity of information is one of the most important aspect of fetal intrapartum surveillance.

FBS may risk a delay in delivering

CTG+ST clinical guidelines provide recommendations on the timing of delivery after significant events have been recorded. Whatever is causing a delay may be regarded as a threat to intact survival. Therefore it is essential to respond quickly when there is sufficient information, and in particular during second stage with active pushing.

In the studies, one of the reasons for a delay in responding was the decision to take an FBS as illustrated by the case presented in Figure 17.

Despite clear indications by emerging CTG changes and progressive rise in T/QRS a decision was made to undertake an FBS which was 6.93. The baby was born one hour after the onset of the hypoxia process in second stage of labour. The importance of recognising the time factor became evident as the 0.01 pH unit fall per minute became clear (**Paper IV**).

With the use of CTG+ST clinical guidelines, significant hypoxic event can be indicated. The current set of data shows the impact of time. Considering that an FBS was obtained in median 14 minutes (range 8-25, 95th CI) after the ST event in 22 out of the 53 cases with marked acidosis it seems appropriate to try to reduce the FBS delay factor as much as possible.

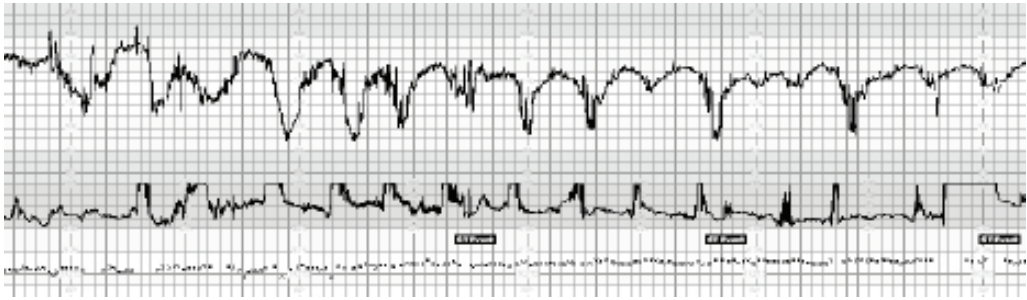


Figure 17. 31-year old para 1, normal pregnancy, induction at 40+1 after 3 days preterm rupture of membranes. Emergency CS for threatening asphyxia at 04:48 after an attempted complicated VE. FBS at 04:21: pH 6.93. Female, BW 3200, Apgar 1-1-3, Cord sample (vein): pH 7.03, pCO₂ 7.4 kPa, BD_{ccf} 14.6 mmol/l. Neonatal resuscitation, on respirator for first 36 hrs. No signs of seizures, normal electroencephalogram.

Thus, the initial experience with CTG+ST+FBS indicated that sufficient information was available from CTG+ST provided the basic requirements for ST analysis were met. At the same time it should be recognised that FBS may be part of the learning-curve with less cases requiring FBS over time.

Non-reassuring CTG at start of ST analysis

Another aspect of particular interest was the relationship between FBS and ST in those cases where CTG changes were noted already at onset of the recording. Even though CTG changes were noted at onset, CTG+ST guidelines indicated abnormality prior to an abnormal FBS in 14 out of 17 cases. The duration between CTG+ST indications to intervene and an abnormal FBS was in median 29 minutes (range 11-74, 95% CI). Of those three cases not identified, two were late onset of the recording in second stage and the third had an FBS obtained nine minutes before a normal vaginal delivery in connection with bradycardia and uterine rupture (cord artery pH 6.97, pCO₂ 15.0 kPa, BD_{ccf} 5.0 mmol/l, normal neonatal period).

Continuing documentation – seven years of ST analysis usage

Most recently, two papers were presented providing each seven years of detailed outcome analysis of CTG+ST usage. In the first, Norén and Carlsson(2008) presented the outcome of CTG+ST usage at Mölndal Hospital. The data covering 22171 term deliveries in active labour showed a marked reduction in cord metabolic acidosis rate in the total population from 0.72% in 2001 to 0.06% in 2007 (p<0.001).

Table XII gives the findings related to cases where a non-reassuring FBS defined as scalp pH <7.20 or scalp lactate >4.7 mmol/l were obtained. Adequate recording with a non-reassuring FBS without CTG+ST indications was always associated with a normal perinatal outcome (no met acidosis and/or 5 minute Apgar >7).

Year	Cases with CTG+ST+FBS	Cases with lactate >4.7 mmol/l or pH <7.20	Distribution of cases with scalp lactate >4.7 mmol/l or scalp pH <7.20					
			Start recording during 2nd stage	Unstable FHR at onset	No ST data available	Interm/abnorm CTG and normal ST in 1 st stage	Interm/abnorm CTG and normal ST in 2 nd stage	ST event before FBS
2001; 2005-06	444	84 (18.9%)	4 (5%)	3 (4%)	9 (11%)	11 (13%)	18 (21%)	39 (46%)
Mean cord art pH			7.15	7.07	7.14	7.23	7.18	7.14

Table XII. Distribution of non-reassuring FBS and corresponding cord artery pH. (p)

Thus, the current data from the Möln dal Hospital show that marked decrease in metabolic acidosis rate was associated with:

- Increased usage of CTG+ST reaching 70%.
- Ability to identify adverse FHR patterns at onset of a recording (lack of reactivity and variability and cases with unstable baseline FHR).
- Ability to respond in time to CTG+ST information (a slow response rate as a cause of metabolic acidosis was found to decrease from 0.75% to 0.09% of all CTG+ST recordings, $p < 0.001$).
- Improved knowledge among staff with regard to CTG+ST assessment due to bedside guidance, repeated teaching sessions in CTG interpretation and intrapartum clinical management as well as the introduction of clinical audit in cases of severe intrapartum asphyxia.
- Improvements in FECG (STAN) technology.

Additional information from FBS was useful;

- When ST analysis was started in second stage.
- When the CTG showed unstable baseline FHR at onset.
- In case of no ST data being available.

The second study contains data from the University of Turku (Timonen 2008). During the last three years and 2040 deliveries monitored with CTG+ST there was only one case with metabolic acidosis (VE for CTG+ST changes, normal neonatal outcome), despite a relatively low operative delivery rate. In the total population, the rate of acidaemia (cord artery pH <7.05) showed a steady decline from 1.5% to 0.7% (OR 0.43, 95%CI 0.27-0.69) at the same time as the FBS rate decreased from the low rate of 1.7% to 0.4% (OR 0.20, 0.14-0.29, $p < 0.0001$).

In summary

Automated ST analysis requires a steady-state situation at onset (a stable baseline and a non-deteriorating FHR pattern) as well as continuous signs of a fetus capable of responding, i.e. signs of reactivity and variability. Provided these prerequisites are fulfilled, the metabolic myocardial stress can be captured identifying the onset of anaerobic metabolism. This enables intrapartum hypoxia to be identified in a timely manner well in advance of asphyxia and in most cases no additional information from FBS is required. However, it has to be emphasized that in the trials included in this thesis, FBS has been used as a complementary methodology and we still lack studies directly evaluating the additional value of FBS, i.e. comparing CTG+ST versus CTG+ST+FBS. The contribution of metabolic acidosis to the lowering of pH is marginal compared to the load of free hydrogen ions caused by accumulation of CO₂. This means that the metabolic component may present itself at different pH levels but the lower the pH, the more likely it is that there is a metabolic acidosis component being added.

What are the exceptions?

Although hypoxia is the most common reason for an adverse outcome of labour, dystocia with related trauma, fetal bleeding and intrauterine infections are also known causes of an adverse outcome where the relationship between fetal pH and ST changes may be different. Recently, a three cases report was published from Westerhuis *et al* 2007. The detailed review identified poor signal quality, difficulties in CTG interpretation, failure to comply with CTG+ST clinical guidelines and deterioration of the CTG without ST events as the leading causes of these adverse outcomes. Interestingly, the report caused Letters-to-the Editor arguing that these cases required additional analysis and ST analysis was not to blame (Ugwumadu 2008, Poddar 2008).

All of these cases had preterminal FHR patterns for different reasons, group-B Streptococcus infection, fetal myocardial dystrophy and maternal hyperventilation causing prolonged QT-intervall (Gyselaers *et al* 2007). This illustrates the fact that fetal surveillance during labour should be about recognising each fetus as an individual and trying to assess the pattern of response (biopattern) associated with each fetus. The current development of residuals to provide on-line information on fetal reactivity features, should be seen as a development along the lines of quantifying fetal reactivity as a key biopattern feature (Rosén *et al* 2007).

Inflammatory reactions in combination with hypoxia are known to cause increased vulnerability of the developing brain (Eklind *et al* 2001) and it is of interest to note that the increase in heart rate variability and ST depression/negative T waves associated with infusion of the bacterial cell fragment lipopolysaccharide in the preterm fetal lamb (Blad *et al* 2008).

Concluding remarks

Fetal surveillance in labour relates to basic (acid base) biochemistry as well as to modern computing and artificial intelligence. Only by working towards improved understanding of mechanisms involved with fetal reactions, or lack of reactions, would we be able to reduce ambiguity, improve and resolve negligence and medico-legal issues. ST analysis of the FECG has been through a rigorous development progress that delivers improved care in perinatal centres keen to participate and adapt. As with all methodologies, nothing is achieved by a piece of machinery, it is the educated monitor using the machinery that makes the difference.

Sammanfattning

Förmågan att rätt bedöma fostrets tillstånd under förlossningen är en utmaning. Vedertagen metod har varit att lyssna på fostrets hjärtfrekvens med stetoskop och, sedan 1970-talet, kontinuerligt följa hjärtfrekvensen med cardiocografi (CTG). Dock har försök utförda både på djur och människa visat att syrebrist under förlossningen kan förändra utseendet på fosters EKG så att en höjning av ”T vågen” och en sänkning av ”ST sträckan” har noterats. En ny medicinsk utrustning (STAN Neoventa Medical, Mölndal) har utvecklats för att analysera foster EKG under förlossningen. I flera randomiserade studier har kombinationen av konventionell CTG tillsammans med analys av ST sträckan visat på lägre frekvens syrebrist hos nyfödda samtidigt som andelen instrumentella förlossningar (kejsarsnitt, tång och sugklocka) kunnat minskas.

Avhandlingens syfte har varit att se hur denna fosterövervakningsteknik har kunnat genomföras i klinisk praxis. På Sahlgrenska sjukhuset i Göteborg har under en period av två år 4830 av totalt 14687 (32,9%) fullgångna graviditeter i aktivt värkarbete följts med ST analys som komplement till CTG. Andelen patienter som övervakades första året var 28,1% och år två 37,7%. En sänkning av andelen barn med syrebrist från 0,76% till 0,44% kunde konstateras hos alla barn under studietiden. I den grupp som var belastad med riskförlossningar och därför följts med ST analys förutom CTG var sänkningen från 1,12% till 0,56%. Andelen operativa förlossningar förändrades ej.

En motsvarande undersökning har utförts på förlossningen i Varberg (år 2004 och 2005). Under denna tid övervakades 59% (1875/3193) med ST analys förutom CTG. Andelen foster med syrebrist var 0,5% av alla förlösta.

Man kan konstatera att andelen foster med syrebrist i denna stora grupp patienter från Göteborg och Varberg (14687+3193) var minst lika låg som tidigare påvisats i gruppen med CTG+ST analys i den svenska randomiserade studien (Amer-Wählin et al 2001).

Fosterblod taget från skalpen (FBS) för analys av pH är ett vedertaget komplement till CTG under förlossning. Utifrån ett material från en europeisk multicenterstudie (omfattande 6999 patienter) angående införandet av ST analys i kliniken, identifierades 911 fall där skalp pH hade tagits.

De flesta (73%) av FBS togs under värkarbetets sista timma för att verifiera CTG och ST förändring. I 14 av de 15 fall med svår syrebrist i navelartären och där barnen togs till neonatal avdelning för observation hade CTG+ST analys indikerat nödvändigheten att förlösa i minst 19 minuter. I de fall förlossning ägde rum inom 16 minuter efter att CTG+ST analys visat patologi sågs i 61% (17/28) navelartär pH >7,20 medan om förlossning skedde efter mer än 16 min hade 19% pH >7,20.

Av de 911 fall där FBS tagits fanns 53 foster som hade pH <7,06 och 44 foster som hade pH mellan 7,06 och 7,09 i navelsträngsartären. I 44/53 fall sågs signifikanta ST förändringar och i två fall var CTG kurvan preterminal (utan reaktion). I fem fall kunde inte CTG+ST analys bedömas fram till 20 minuter innan förlossning och i fem fall visade CTG+ST analys inga indikationer att ingripa. Ett av dessa fall hade svår syrebrist. I pH 7,06-7,09 gruppen indikerade ST analysen skäl att ingripa i 24 fall. Av de 20 fall utan ST analys förändring hade alla Apgar minst sju, utom ett barn som förlöstes med sugklocka. Detta barn hämtade sig snabbt.

I fall av patologiskt CTG och skalp pH <7,20 identifierade ST analys abnormitet före FBS i alla fall utom sju. Ingen av dessa sju fall hade senare svår syrebrist. I två % av fallen sågs falskt positiv ST analys.

Sammanfattningsvis pekar dessa studier på att fosterövervakning med ST analys av foster EKG även i klinisk praxis kan minska antalet barn som föds med syrebrist och att ST analys liksom FBS är ett bra komplement.

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