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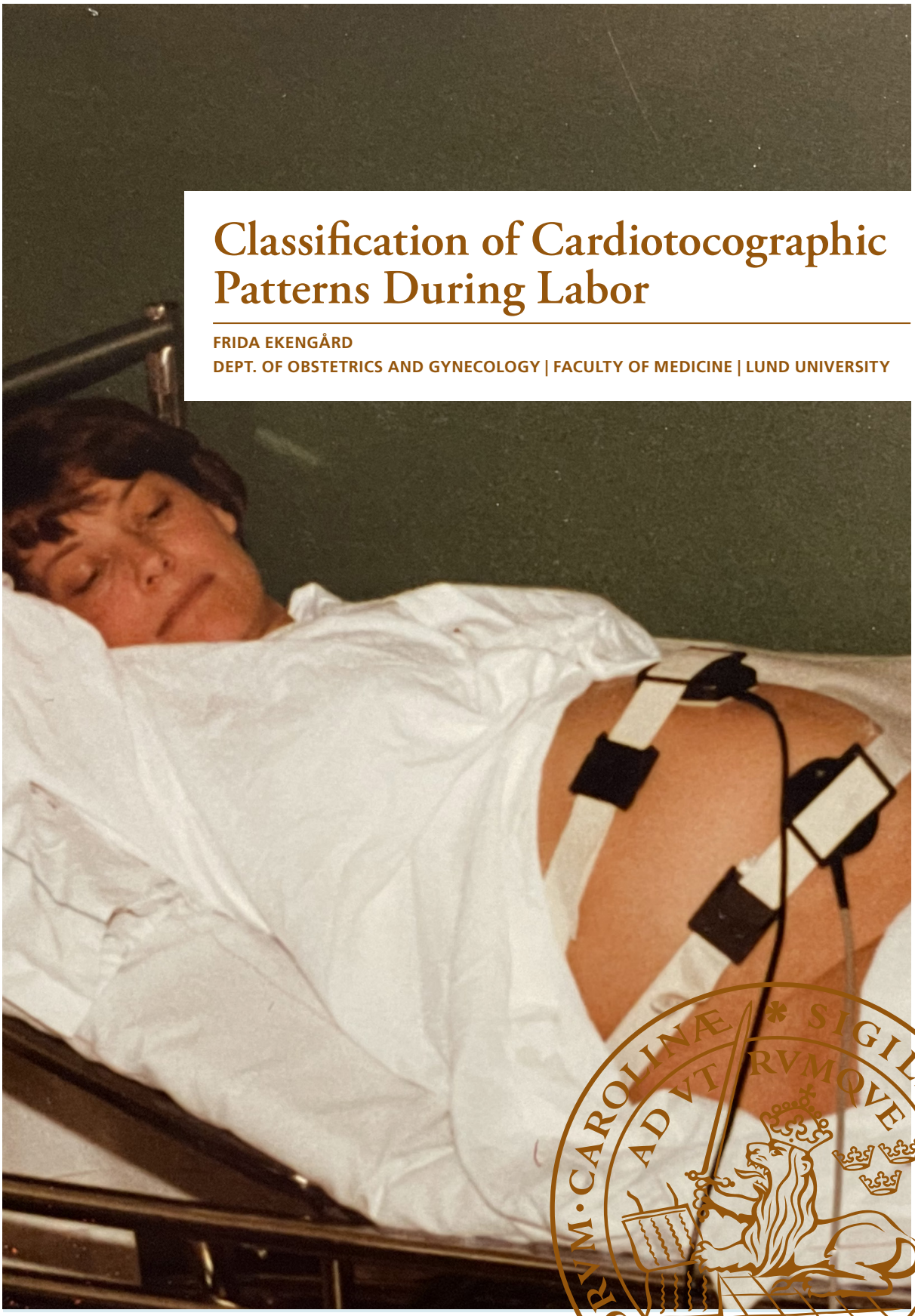

Classification of Cardiotocographic Patterns During Labor

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Frida Ekengård

LUND
UNIVERSITY

DOCTORAL DISSERTATION

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Abstract:

Background

CTG is the main method of fetal surveillance during labor. When CTG is used, different guidelines are used to help with the interpretation. A new international guideline was presented by FIGO in 2015 without prior evaluation and was implemented in a modified version in Sweden in 2018. The aim of this thesis was to evaluate the two new templates and the former Swedish template and their usefulness during labor.

Methods

In Paper I and Paper II CTG tracings from neonates born with acidemia in the first and second stage of labor and CTG tracings from corresponding controls without acidemia were interpreted by midwives and physicians. The sensitivities and specificities for identifying acidemia were calculated. In Paper III one of the variables that differs between the templates, accelerations, was examined and OR for acidemia calculated for the presence of different types of accelerations. In Paper IV the sensitivity and specificity for perceived need for intervention after using the two Swedish templates was examined, as well as agreement between perceived need for intervention and classification according to the template.

Results

The new international template classifies many tracings, from from neonates with and without acidemia, as suspicious. It has a low sensitivity to identify acidemia in both stages of labor for classification pathological. The former Swedish guideline has a high sensitivity in both stages, but a lower specificity in the second stage. The new Swedish guideline has a low sensitivity for the classification pathological. For the combination of pathological and suspicious patterns the sensitivity is higher, without losing too much specificity. The guideline in use affects the decision making and current residents consider a tracing classified as pathological as a need for intervention. Sporadic accelerations are a strong sign of wellbeing whereas the lack of sporadic accelerations is a weak sign of pathology. Periodic accelerations are not a strong sign of wellbeing of the fetus.

Conclusion

The new international guideline is not safe to use, due to a too low sensitivity. The former Swedish guideline had the highest sensitivity, but a low specificity in the second stage of labor, risking unnecessary interventions. With the current Swedish guideline awareness must be raised for suspicious tracings, that may warrant a need for intervention. The presence of sporadic accelerations is a strong sign of wellbeing of the fetus, whereas periodic accelerations are not.

Key words: Fetal Monitoring, Carditocography, Classification, Delivery, Asphyxia, Accelerations

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To my Beloved Family

The greatest enemy of knowledge is not ignorance; it is the illusion of knowledge.

Stephen Hawking

Table of Contents

Abstract

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The new international template classifies many tracings, from neonates with and without acidemia, as suspicious. It has a low sensitivity to identify acidemia in both stages of labor for classification pathological. The former Swedish guideline has a high sensitivity in both stages, but a lower specificity in the second stage. The new Swedish guideline has a low sensitivity for classification pathological. For the combination of pathological and suspicious patterns the sensitivity is higher, without losing too much specificity. The guideline in use affects the decision making and current residents consider a tracing classified as pathological as a need for intervention.

Sporadic accelerations are a strong sign of wellbeing whereas the lack of sporadic accelerations is a weak sign of pathology. Periodic accelerations are not a strong sign of wellbeing of the fetus.

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Populärvetenskaplig sammanfattning

CTG, kardiotokografi, är en metod som används för att övervaka det ofödda barnets hjärtrytm. CTG används både under graviditet och under förlossning. Barnets hjärtrytm registreras och frekvensen ritas upp på papper eller på skärm som en graf, CTG. Denna graf behöver sedan tolkas. När vi tolkar CTG försöker vi förstå hur barnet i magen mår.

CTG utvecklades på 50-talet och studerades sedan under 70-90 talet. Man fann att antalet barn som fick kramper i nyföddhetsperioden minskade med 50% med CTG övervakning men i övrigt var det svårt att bevisa att CTG gjorde nytta. Dock har antalet barn som dör under förlossningen minskat sedan införandet.

När vi använder CTG gäller det att vi tolkar/förstår barnets hjärtrytm rätt. Det vi vill är att hitta barn som mår dåligt under förlossningen, barn som inte har kapacitet att klara av de krafter en förlossning utgör. Om man misstänker att för många barn mår dåligt kommer det att leda till för många onödiga ingrepp, som kejsarsnitt och instrumentell förlossning, som kan påverka både mamman och barnet negativt. Om vi inte hittar de barn som mår dåligt riskerar de att dö under förlossningen eller födas med syrebrist som kan ge handikapp för livet.

När barnen föds tas oftast blodprover från navelsträngen. Detta blod är barnets blod. Om barnet har utsatt för en syrebrist i magen sjunker pH värdet i barnets blod. Nyfödda barn klarar mycket lägre pH värden än vuxna. I en vuxens blod är pH värdet kring 7.4. Nyfödda barn kan ha betydligt lägre pH värde och ändå må alldeles utmärkt. Vilka gränser som används för att säga att barnet har utsatts för en syrebrist varierar, men barn som har pH över 7.15 mår oftast alldeles utmärkt. Om pH värdet är under 7.0 finns det en risk att barnet kommer att få men av syrebristen.

När vi bedömer en CTG kurva tittar vi på olika saker. När det gäller barnets hjärtrytm så tittar vi på hur den förändras över tid och hur rytmen påverkas av mammans värkar. Vi bedömer olika variabler av CTG. Variablerna som berör hjärtrytmen hos barnet kallas för basalfrekvens, variabilitet, accelerationer och decelerationer. Dessutom bedöms moderns värkar.

När CTG infördes och de flesta studier gjordes fanns inga internationellt gemensamma hjälpmedel i hur man skulle tolka graferna. 1987 publicerade FIGO, som är en världsorganisation för förlossningsläkare och gynekologer, en riktlinje som skulle hjälpa till vid tolkningen av CTG under förlossning. Denna riktlinje

spreds över världen och förändrades i olika länder. I Sverige användes en variant av denna som i avhandlingen kallas SWE09.

2015 publicerade FIGO en ny mall för tolkning av CTG kurvor under förlossning, den kallas i avhandlingen för FIGO15. Denna mall togs fram av en panel av kunniga i CTG från hela världen. Dock valde man att publicera den och rekommendera att den skulle användas innan den hade utvärderats i sin helhet. I Sverige valde man att göra en variant av denna mall, som här kallas SWE17. Denna mall valde man också att införa i verksamheterna i Sverige utan att utvärdera den först.

När den nya internationella mallen infördes 2015 valde vi att påbörja detta projekt. Målet var att utvärdera den mall som användes i Sverige då och jämföra den med den nya internationella. När man sedan valde att införa den nya svenska mallen utan utvärdering inkluderade vi den i våra studier. Nu hade vi tre mallar att jämföra och se vilken som var säkrast att använda under förlossning, SWE09, FIGO15 och SWE17.

Med dessa tre mallar så bedöms de olika delarna av CTG kurvan och sedan gör man en slutgiltig bedömning där kurvan klassificeras som normal, avvikande eller patologisk. Om kurvan bedöms som normal bedömer man att barnet mår bra. Om den är avvikande finns det viss risk för barnet och om den är patologisk är det stor risk att barnet utsätts före syrebrist. När man bedömer hur bra en mall är så tittar man på hur många av barnens kurvor som hamnar i rätt kategori. Med en perfekt mall hade alla barn med syrebrist haft CTG kurvor som klassificerades som patologiska och alla barn utan syrebrist hade haft kurvor som klassificerades som normala.

CTG är känt för att ha ett högt negativt prediktivt värde, NPV, dvs om CTG kurvan bedöms som normal är risken för att barnet har syrebrist mycket liten, men vi misstänker att många barn som mår alldeles utmärkt inte gör det (lågt positivt prediktivt värde, PPV). Detta kan leda till att barn förlöses med kejsarsnitt eller med sugklocka i onödan. Att hitta en mall som hjälper oss att hitta rätt barn är viktigt.

Denna avhandling innehåller fyra delarbeten.

Delarbete I

I det första delarbetet studerades CTG kurvor från slutet av förlossningen, utdrivningsskedet. Denna del av förlossningen är den som är mest riskfylld för barnet. Utöver värkarna utsätts barnet även för att mamman krystar och ofta har barnet varit utsatt för förlossningsvärkar under många timmar vilket kan ha orsakat att dess resurser börjar ta slut. Att bedöma CTG kurvor under utdrivningsskedet är svårt.

I studien bedömdes kurvor från barn som föddes med sänkt pH värde i blodet vid födseln med kurvor från barn som hade normala pH värden vid födseln. Totalt bedömdes CTG kurvor från 295 barn födda med låga pH värden och från 591 barn

utan sänkta pH värden. Dessa kurvor bedömdes av tre olika personer, både läkare och barnmorskor, som jobbar på förlossningsavdelningar. Utifrån deras bedömningar beräknades sedan hur bra mallarna var på att hitta rätt barn, dvs de barn som behövde hjälp för att inte riskera att ta skada av förlossningen, men utan att felaktigt identifiera syrebrist hos barn med normal syresättning och därmed riskera onödiga ingrepp.

Den nya internationella mallen bedömdes inte säker att använda. Alldeles för många kurvor blev klassificerade som avvikande vilket gav en låg sensitivitet. Den gamla svenska mallen var bra på att hitta de barn som hade låga pH värden, dvs hade hög sensitivitet, men den hade en låg specificitet vilket ökar risken för onödiga ingrepp. Den nya svenska mallen hade också en låg sensitivitet men en högre specificitet. Sensitiviteten om man bara reagerar på kurvor som var klassificerade som patologiska var för låg för att vara säker att använda. Om man däremot valde att räkna in kurvor som klassificerades som avvikande hade mallen en bra sensitivitet och specificitet.

Delarbete II

I delarbete II studerades kurvor från första delen av förlossningen. Denna del kallas öppningsskedet och det är då livmodertappen öppnar upp sig för att göra plats för barnets passage. Denna del av förlossningen kan vara lång och om man behöver avbryta förlossningen är det bara möjligt att göra med kejsarsnitt.

I denna studie studerades CTG kurvor från barn som föddes med akuta kejsarsnitt under öppningsskedet och som hade sänkta pH värden i navelsträngsblodet vid födseln. Dessa CTG kurvor jämfördes med CTG kurvor från samma öppningsgrad av livmodertappen hos barn som föddes utan sänkta pH värden. Total bedömdes CTG kurvor från 73 barn med låga pH värden och från 219 barn utan sänkta pH värden vid födseln.

Även i denna studie visades att den internationella mallen vara för osäker för att användas i förlossningsvården. Den gamla svenska var den som bedömdes säkrast att använda. När den nya svenska mallen används är det viktigt att man reagerar även på avvikande mönster, men den nya svenska mallen missade även då något fler barn med sänkta pH värden.

När man tittade på delarbete I och II ihop och tittade på vilka barn som hade fötts med låga pH värden så fann vi att i första delen av förlossningen var det en högre del av barnen som föddes med låga pH värden som var från förlossningar som kunde klassificeras som högrisk. I utdrivningsskedet sågs igen sådan skillnad. Det fanns en risk att drabbas av syrebrist och låga pH värden även om det var en lågriskförlossning.

Delarbete III

När de två första studierna hade slutförts så hade vi funnit att de olika mallarna skiljde sig åt och att de klassificerade kurvor olika samt att de hade olika sensitivitet och specificitet. Det var dock så att ingen av dem var perfekt. För att gå vidare valde vi därför att börja titta på de olika delarna av CTG för att se vad vi bedömde var viktigt att ha med i en eventuell ny mall.

I delarbete III undersöktes accelerationer. Accelerationer är uppgångar i barnets hjärtfrekvens. Accelerationer sägs vara ett bra tecken i en CTG kurva. Det är dock inte alla uppgångar i barnets hjärtfrekvens som är denna typ av accelerationer. I delarbete III delades accelerationerna upp i två sorter. Dels de som kom sporadiskt, när som helst, dels de som kom i samband med att mamman hade en värk, periodiska. De som är sporadiska uppkommer oftast på grund av att barnet rör sig, medan de som är periodiska troligen beror på kompression av navelsträngen vid värk. Vi tittade sedan på vad det innebar att dessa två typer av accelerationer fanns i CTG kurvan och dels vad som kunde påverka om det fanns accelerationer eller inte.

Om det finns sporadiska accelerationer i en CTG kurva är detta ett bra tecken som i princip utesluter att barnet har tecken på syrebrist. Dock är frånvaro av accelerationer ett otydligt tecken. Även många av de barn som mår alldeles utmärkt fattas accelerationer i sin CTG kurva. Det är skillnad i början och i slutet av förlossningen. I början av förlossningen är det en starkare varningssignal om det fattas accelerationer än i slutet av förlossningen. Periodiska accelerationer var inte ett säkert tecken på att barnet mådde bra. Således är det viktigt att avgöra vilken typ av accelerationer som förekommer i CTG kurvan vid tolkning.

Delarbete IV

Efter att vi har bedömt en CTG kurva under förlossning tar vi beslut om hur vi ska gå vidare. I delarbete IV undersöktes om de beslut som tas förändras beroende på vilken CTG mall som används. Även samstämmigheten mellan klassificeringen med mallen och det beslut läkaren som granskade kurvan i efterhand ville ta undersöktes. I denna studie användes de tolkningar som gjordes av ST läkare i de första delstudierna. Dessa CTG kurvor fick tolkas igen av nya ST läkare. De ST läkare som tolkade i de två omgångarna hade i sitt arbete enbart använt den mall som de använde i studien.

ST läkarna tog olika beslut beroende på vilken mall de använde. Med den gamla svenska mallen tog de oftare beslut om att de behövde ingripa när barn hade låga pH värden än med den nya svenska mallen, men de ville även ingripa i fler fall där barnen inte hade låga pH värden. ST läkarna som använde den nya svenska tolkningsmallen hade stor samstämmighet mellan beslut att vilja ingripa och att de tolkade kurvan som patologisk. De ville inte ingripa lika ofta om kurvan tolkades som avvikande. Studien visade gällande klassificering av kurvorna ungefär samma

resultat som delarbete I och II, det vill säga att den gamla svenska mallen var bättre på att hjälpa oss att hitta barn som inte mår bra, medan den nya mallen var bättre på att hjälpa oss att undvika onödiga ingrepp. Om man räknade in avvikande mönster i behov att ingripa var den nya mallen också bra. Det var dock inte så att ST läkarna tog med avvikande mönster som grund för ingripande lika ofta i sina beslut.

Nyhetsvärde

Sammanfattningsvis visar studierna i denna avhandling att de olika tolkningsmallarna är olika. Den svenska gamla mallen var bra på att hitta barn som mådde dåligt men ökade risken för onödiga ingrepp i slutet av förlossningen. Den nya svenska mallen minskar risken för onödiga ingrepp, men ökar risken för att vi missar barn som mår dåligt. Detta gäller särskilt om man inte reagerar även på avvikande kurvor. Den internationella nya mallen är för trubbig för att kunna användas säkert. För många kurvor klassificeras som avvikande för att den ska vara användbar. Vilken mall som används påverkar även vilka beslut som tas och i nuläget finns det en risk att barn som mår dåligt missas på grund av att man väljer att inte ingripa när kurvor bedöms som avvikande.

Om det finns sporadiska accelerationer i CTG kurvan kan man med betydande säkerhet dra slutsatsen att barnet mår bra, om det inte efter dessa händer något allvarligt. Om man ser sporadiska accelerationer behöver man inte vara orolig, men om det inte finns accelerationer behöver det inte innebära att barnet mår dåligt, men det kan vara av värde att fortsätta övervakningen och vara observant på förändringar, särskilt i början av förlossningen.

List of Papers

Paper I

Ekengård F, Cardell M, Herbst A. Low sensitivity of the new FIGO classification system for electronic fetal monitoring to identify fetal acidosis in the second stage of labor. Eur J Obstet Gynecol Reprod Biol X. 2021; 9:100120.

Paper II

Ekengård F, Cardell M, Herbst A. Impaired validity of the new FIGO and Swedish CTG classification templates to identify fetal acidosis in the first stage of labor. The journal of maternal-fetal & neonatal medicine. 2021:1-8.

Paper III

Ekengård F, Cardell M, Herbst A. Sporadic accelerations during labor strongly indicate normal pH, whereas periodic accelerations do not: a case–control study. The Journal of Maternal-Fetal & Neonatal Medicine. 2022:1-8

Paper IV

Ekengård F, Cardell M, Herbst A. CTG interpretation templates affect residents' decision making. *Submitted*

Preface

In the 1830's the fetus' heart rate was determined with a stethoscope and thoroughly described. The frequency and how it was altered during delivery was known. One hundred and twenty years later the fetal heart rate during labor were to be explored with CTG, cardiotocography.

Since the introduction of CTG as a surveillance method, many studies have been performed. It has been found that the rate of neonatal seizures is lowered with CTG monitoring but the impact on perinatal and neonatal death has been debated, and the rate of cesarean deliveries has risen. However, since the introduction of CTG the rate of neonatal mortality has fallen. CTG is a diagnostic method, not a therapy that directly prevents asphyxia. The efficiency in preventing asphyxia is therefore reliant on the interpretation of the fetal heart rate patterns as well as on actions taken when these patterns indicate impending asphyxia.

In 1987 the first international guideline on how to interpret the CTG tracings was published by FIGO, The International Federation of Gynecology and Obstetrics, the FIGO87. The FIGO87 was adapted in various forms over the world. Other guidelines were also developed. The various guidelines made it hard for international comparison of the effectiveness of CTG and the FIGO87 was thought to increase the rate of cesarean deliveries.

In October 2015 FIGO published a new international guideline, the FIGO15. It was the result of a consensus panel and unfortunately, it was not evaluated as a template before the introduction. We decided that we wanted to evaluate the template and compare it to the guideline that was used in Sweden at that time, SWE09. We wanted to conduct these studies before the implementation in Sweden. A Swedish group of obstetricians and midwives decided that the implementation could not await studies and the SWE17, a modified version of the FIGO15, was introduced in 2017 and implemented in 2018. The SWE17 was also introduced without prior studies of the specific template. It was unknown how this would influence the wellbeing of our newborns and mothers. Therefore, we decided to include the SWE17 in our studies.

The first aim of our studies was to find out which guideline that is the safest to use in labor. With a low risk of missing fetuses at risk of asphyxia without too many unnecessary interventions. And a secondary aim was to create a new guideline for a safer intrapartum fetal surveillance. Paper I, II and IV are a part of the evaluation of

the three guidelines and Paper III is part of a more detailed evaluation of the variables of the CTG with the aim to develop an improved guideline further on.

Abbreviations

ACOG	American College of Obstetrics and Gynecology
bpm	Beats per minute
CD	Cesarean delivery
CI	Confidence interval
cm	Centimeter
CO_2	Carbon dioxide
CTG	Cardiotocography
ECG	Electrocardiogram
FBS	Fetal blood sampling
FSS	Fetal scalp stimulation
FHR	Fetal heart rate
FIGO	The International Federation of Gynecology and Obstetrics
FIGO15	The FIGO CTG guideline from 2015
FIGO87	The FIGO CTG guideline from 1987
HIE	Hypoxic ischemic encephalopathy
IUGR	Intrauterine growth restriction
IUPC	Intrauterine pressure catheter
LÖF	The health care regions common insurance company
min	Minute
NICE	National Institute for Health and Care Excellence
NO	Nitric oxide
NPV	Negative predictive value
OR	Odds ratio
PPV	Positive predictive value
RCOG	The Royal College of Obstetricians and Gynaecologists
RCT	Randomized controlled trial
SFOG	The Swedish Society of Obstetrics and Gynecology
STAN	ST-analysis of the fetal ECG
SWE09	The Swedish CTG guideline from 2009
SWE17	The Swedish CTG guideline from 2017

Introduction

History and evidence of CTG

The fetus' heartbeat was described in 1833. In Kennedy's book, "Observations on obstetric auscultation" it was reported that with a stethoscope the heart rate of the fetus could be determined. He described that the fetus normally had a heart frequency between 130 and 140 bpm but that it was altered by the uterine motions during delivery and by the mothers' state of mind. He also described that when the heart frequency of the fetus fell there was a risk for the fetus' wellbeing and that a rise in frequency was seen when fetal movements were palpated (1).

In the 1950s an electronic technique of surveillance of the fetal heart rate was developed, cardiotocography, CTG (2). It was developed parallel to fetal blood sampling, FBS. FBS, measuring pH, was first introduced into clinical practice. However, CTG was more practical and less invasive and spread quickly as a method of fetal surveillance. The rate of perinatal mortality fell after the introduction of CTG at British delivery wards making it ethically difficult to perform randomized trials, but the fall in perinatal deaths were multifactorial (3) and trials were later performed.

In the 1970s to the 1990s randomized clinical trials, RCTs, of CTG were carried out but the effectiveness of the method was hard to prove, even though a reduction of neonatal seizures was found (4, 5, 6, 7, 8, 9, 10). A reduction of perinatal mortality and long-term sequels has not been proven and the rate of obstetric interventions has increased (11, 12, 13, 14, 15). A Swedish study did not find an increase in cesarean deliveries, CD, due to fetal distress when CTG was combined with FBS in low risk deliveries (16). Population based studies have indicated that surveillance with CTG is associated with a decrease in neonatal mortality and morbidity (17) and the use of CTG may not prevent all cases of asphyxia but may prevent the progression from mild to severe asphyxia (18).

The RCTs of CTG were carried out in a clinical practice that differ a lot from current practice, and they were underpowered for evaluation of perinatal death and long-term morbidity (8, 19). A recent review concluded that intermittent auscultation reduces emergency CD, without increasing the risk for adverse outcomes. The study included 33 randomized trials studying different ways of fetal surveillance. The studies that included intermittent auscultation were all old studies except one from

Tanzania (20). The study from Tanzania was conducted in a rural hospital without CTG available (21). So even if it was a new review the included studies were the same as in prior studies and still with the disadvantages mentioned above. Since it has been hard to prove the benefits of CTG there is still differences in opinion if it should be used or not (22).

The rise in CD is not only due to the implementation of CTG. There has been changes in the demands from mothers, financial and logistic incentives, and a fear of legal consequences if there are complications during vaginal delivery (23).

It has been claimed that CTG is a method with high sensitivity but where pathological patterns have a low specificity for neonatal hypoxia, which may lead to unnecessary interventions. The effectiveness of CTG for other outcomes than reducing neonatal seizures has not been proven. Still, it is now the main method of fetal surveillance in delivery wards in many countries. (19).

The first international guidelines of CTG were introduced by FIGO in 1987, FIGO87 (24). They were modified to different guidelines in different countries over the years leading to classification systems that differ in their classification of the same tracing (25, 26). In Sweden a national classification template, the SWE09, was in use between 2009 and 2017 (27). It was a modification of the FIGO87 and the STAN guideline from 2007 (24, 28).

Later it was stated that the FIGO87 guideline had limitations and that there was a need for a new international guideline that needed to be simpler and more objective and with clearer associations between classification and clinical management (29). The lack of an international guideline was thought to lower the effectiveness of CTG (26). Therefore a consensus panel began working on a new international guideline that was introduced in 2015, FIGO15 (19). A modified version of the international template was introduced in Sweden in 2017, SWE17 (30) and implemented in 2018. The old template was thought to have a low specificity that might have caused not needed interventions and there was a desire to adapt to international guidelines (31). In Denmark and Norway, it was decided to not adopt the new international guidelines since there were no evidence for their effectiveness (32, 33, 34). There was not a scientifical evaluation of neither of the templates, FIGO87, SWE09, FIGO15 and SWE17, before the implementation in clinical practice. They were all based on consensus panels.

After the introduction of the FIGO15 and the SWE17 they have been compared to older templates in different studies.

Olofsson et al have compared the FIGO15 and the SWE17 to the STAN interpretation template from 2009. They found that the classification differs with what template that is used and that that the FIGO15 has a lower sensitivity to identify neonates with acidemia than the STAN template (35, 36). Coletta et al compared a five tier system to a three tier system, similar to the FIGO15, and found

a low sensitivity of the three tier system since most cases and controls were classified as category 2, suspicious (37). Another study compared the FIGO15 to the Nice guidelines from 2007 and 2014. The FIGO15 led to a moderate rate of interventions and was easy to use, but they did not look at the outcome of the neonate and the validity of the classification (38).

In 2021 a study by Zamora del Pozo et al compared four different guidelines, FIGO15, ACOGs guideline, the NICE guideline and the Chandraharan guideline. The Chandraharan guideline differ from the other three since it is said to have a physiological approach to the CTG. They found that there was no significant difference between the four guidelines, they all had a moderate capacity to predict acidemia (39).

The variables of CTG

The CTG is assessed according to the CTG variables; baseline, variability, accelerations, decelerations, and contractions, Figure 1.

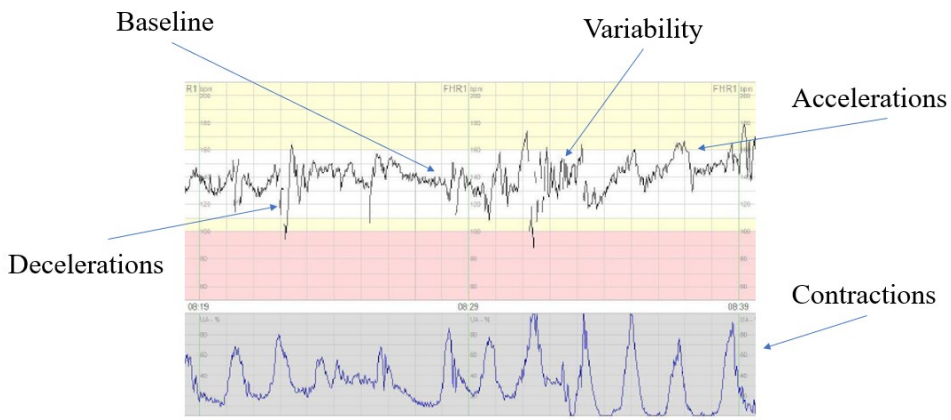


Figure 1. CTG variabels
The variables of the CTG; baseline, variability, accelerations, decelerations, and the contractions.

Baseline

The baseline fetal heart rate is the mean level of the fetal heart rate, accelerations and decelerations excluded. Five to ten minutes is needed to determine the baseline. The baseline is regulated by the autonomous part of the nervous systems; the parasympathetic part lowers the basal heart rate and the sympathetic part increases it (40).

Preterm fetuses have a higher normal range than full term fetuses and post term fetuses has a lower normal range (41, 42, 43, 44, 45). These are all studies of the antepartum fetal heart rate and not during labor. In the Swedish guidelines the classification of the baseline only differs according to gestational age in the antepartum classification (31). A reason for the higher fetal heart rate of preterm fetuses is thought to be that the parasympathetic part of the autonomic nervous system develops later than the sympathetic part (40).

Guidelines state that a normal fetal heart rate for full term fetuses is 110-160 bpm (19, 30, 46, 47). The older guidelines, FIGO87, SWE09 and the STAN guideline from 2007 stated the normal range at 110-150 bpm (24, 27, 28).

A fetal heart rate above the normal range is called tachycardia. The guidelines differ in if tachycardia is suspicious at the most (19, 30, 47) or if a tachycardia above 170-180 bpm renders a pathological classification (24, 27, 28, 46). Tachycardia may be caused by maternal factors, e.g., fever and chorioamnionitis, or neonatal factors, e.g., activity, hypoxia/acidemia, or infection (31, 40, 48, 49, 50).

Bradycardia is a fetal heart rate baseline below the normal range. The intermediate range 100-110 bpm is classified suspicious (19, 24, 27, 28, 30, 46) or pathological (47) depending on guideline, whereas all guidelines agree regarding that a bradycardia below 100 bpm renders a pathological pattern. Bradycardia may be caused by an acute obstetric mechanical event such as abruption or uterine rupture. It may also be caused by hypoxia or a worsening of an existing hypoxia (31). If a bradycardia cannot be reversed, delivery is recommended (19, 30).

The baseline is said to be the most important variable in CTG interpretation and needs to be established before the CTG is interpreted. A change in baseline, less than 50 % of the time at the baseline, or an unstable baseline are all warning signs when interpreting CTG tracings (51). Bradycardia before birth is associated with birth asphyxia (11, 52, 53).

Variability

Variability is the variation of the fetal baseline, not including accelerations and decelerations. The bandwidth over one-minute segments decides the variability. The variability is affected by the autonomic nervous system, where the parasympathetic part lowers the amplitude and the sympathetic part increases the amplitude (54, 55). Short term variability can only be assessed by computer and is only used in interpretation algorithms before the onset of delivery (31).

The variability differs depending on gestational length. The variability increases during pregnancy up till week 41+0, where it decreases. The change is due to maturity of the central nervous system of the fetus (41, 45).

Guidelines agree on that a normal variability is 5-25 bpm. A normal variability means that the autonomic nervous system is intact (40).

A reduced variability, less than five bpm, can be a sign of distress of the fetus. Periods of deep sleep may also lower the variability but will be followed by normal variability (40). An isolated low variability is usually not a sign of hypoxia (56). The reduced variability is classified as suspicious or pathological with guidelines (19, 24, 27, 28, 30, 46, 47) depending on the length of the period and other discrepancies of the CTG.

An increased variability, also named saltatory pattern, more than 25 bpm, lasting for a longer period may also be a sign of distress of the fetus, but is poorly understood. It may be caused by an instability of the autonomic nervous system (19, 57). Increased variability during the last 30 minutes of labor is associated with respiratory distress and metabolic acidosis of the neonate (57, 58). However, an increased variability lasting for more than 30 minutes is a very rare pattern, and it may be more interesting to look at shorter periods of high variability (59). In guidelines an increased variability for a longer period is classified as suspicious (24, 27, 28, 47) or pathological (19, 30, 46).

Some guidelines state that an absent variability, less than two bpm, is a severe warning sign needing rapid intervention (27, 28, 30). It is strongly associated with asphyxia (60, 61) and is a late sign in the hypoxic process (40).

Sinusoidal pattern is a pattern that resembles a sine wave. It has a frequency of three to five cycles per minute and an amplitude of 5-15 bpm. The pattern continues for more than 30 minutes and there are no accelerations present. It is seen in severely anemic fetuses or in acute fetal hypoxia. Shorter periods of a sine like pattern can be seen during fetal thumb sucking, this pattern however, is not consistent and it is harmless (19).

Accelerations

An acceleration is a temporary rise of the fetal heart rate above the basal heart rate. In term fetuses an elevation of 15 bpm and a duration of 15 seconds is needed for the rise to be defined as an acceleration (19, 46, 47). Accelerations occurring without correlation to uterine contraction may be classified as sporadic whereas those occurring simultaneously with contractions may be considered periodic (62, 63, 64). Example of sporadic and periodic accelerations are seen in Figure 2.

In the CTG of preterm fetuses a lower amplitude (10 bpm) and shorter duration (10 seconds) is needed to define a rise as an acceleration (19, 31). The number of accelerations per 30-60 minutes increases with gestational age (41, 45, 65, 66). Accelerations are a positive sign in the CTG tracing. Fetuses with accelerations in the first stage of labor have a normal pH at FBS (67). The absence of accelerations

is associated with fetal hypoxia and neonatal encephalopathy and has a higher association to fetal acidemia than a category II (suspicious) tracing (68, 69, 70, 71). In the antepartum CTG of a term fetus accelerations are needed for normality (31) whereas the lack of accelerations during active delivery is said to be unspecific and common (19, 31).

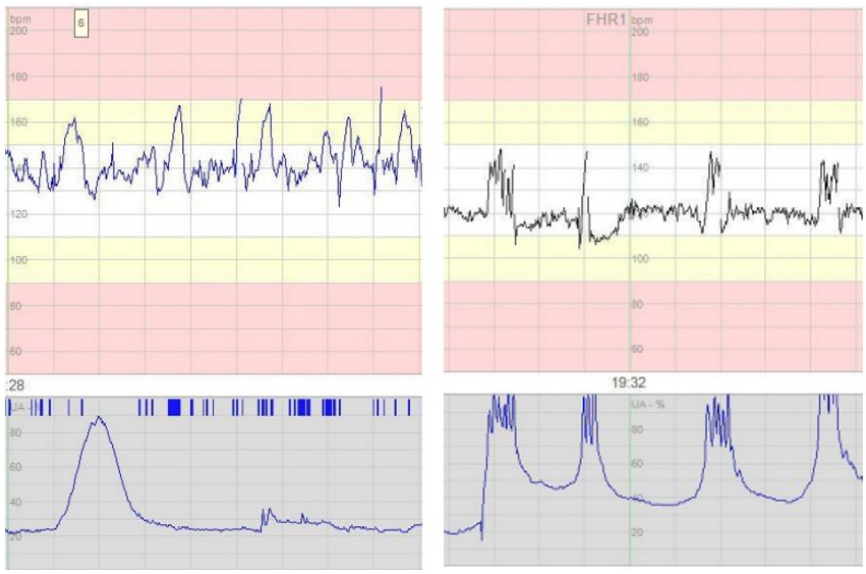


Figure 2. Accelerations
Sporadic and periodic accelerations.

Krebs declared that sporadic and periodic accelerations differ and that it is the sporadic accelerations that is a positive sign of the CTG (62). Periodic accelerations occur simultaneously with contractions and may be an early sign of compression of the umbilical cord (72). Sporadic accelerations are shown to occur simultaneously to fetal movements (49, 73, 74) and are controlled by the somatic nervous system (40). Accelerations coinciding with contractions may also be erroneously monitored maternal pulse since the maternal pulse often increases during contraction (75, 76, 77). It is important when assessing a CTG tracing to remember that all rises in fetal heart rate is not true accelerations and a health sign of the fetus (78).

In current national and international guidelines accelerations are not classified as sporadic or periodic and accelerations are not needed for the classification normal (19, 30, 46, 47) during delivery. The SWE17 has specific guidelines for antepartum classification, where accelerations are required for classification normal from week 28 (31). The SWE09 and the STAN guideline from 2007 demanded accelerations for classification normal during delivery (27, 28).

Decelerations

A deceleration is a transient decrease in fetal heart rate below the baseline of at least 15 bpm, lasting for at least 15 seconds (19). They can be caused of a mechanical or a hypoxic stress of the fetus (40).

Early decelerations are mediated by fetal head compression and are seen at the same time as contractions. They are not thought to be a sign of fetal hypoxia (19). Variable decelerations are V-shaped and baroreceptor-mediated. They are caused by umbilical cord compression and not often associated to fetal hypoxia unless they are severe (19, 40, 56). Late decelerations are more U-shaped and occur late compared to the contractions. They are chemoreceptor mediated. They may be a sign of fetal hypoxia (19, 56) and have been associated to subsequent cerebral palsy (79).

In early pregnancy variable decelerations with short duration are normal whereas decelerations of other forms are a warning sign (31, 41, 80). After 34 weeks, decelerations are not normal in the antepartum period (31).

The guidelines differ in their classification of decelerations. They differ in their definition of decelerations, and the severity of classification with different decelerations present. The FIGO15 demands no repetitive decelerations for category normal (19), the NICE guideline approves variable decelerations with no concerning characteristics for classification normal (46) and the ACOG guideline accepts early decelerations for classification normal (47). For classification pathological it differs even more but most guidelines agree on that repeated late decelerations and prolonged variable decelerations are matters of concern (19, 27, 28, 30, 46, 47).

Contractions

Cardiotocographic tracings include the fetal heart rate and the contractions of the uterus. The frequency of contractions is measured as contractions per ten minutes (19, 81). A normal frequency is three to five contractions per ten minutes whereas tachysystole is more than five contractions per ten minutes averaged over 30 minutes (19, 81).

The contractions compress the vessels in the uterine wall as well as the umbilical cord. This can cause a disturbance in the gas exchange between the mother and fetus. If there are no pauses between the contractions the fetus can be at risk for developing asphyxia (81, 82, 83). Tachysystole is a recognized cause of birth asphyxia (84, 85) and increased uterine activity both in the first and second stage of labor is associated with birth asphyxia (86).

In the SWE09 contractions were a part of the classification template (27), whereas it is not in other templates (19, 28, 30, 46, 47). However, the contractions need to be recorded for correct classification of decelerations.

Monitoring with CTG

Surveillance with CTG is used both antepartum and during delivery (31). The CTG tracings antepartum are changing with gestational age and vary in growth restricted fetuses (41, 42, 87). The focus of this thesis is intrapartum surveillance with CTG why the antepartum CTG won't be thoroughly described.

Internal and external monitoring

External monitoring of the fetal pulse is mediated by doppler ultrasound. It can be used during pregnancy and delivery. After the rupture of membranes an internal electrode, attached to the fetus presenting part, can be used that identifies the R waves of the fetal electrocardiogram (19).

External monitoring increases the risk of misidentification of the mother's pulse as fetal and causes a higher rate of signal loss (75, 88) whereas internal monitoring increases the risk of transmission of blood borne infectious diseases (89).

The contractions are monitored with a tocodynamometer placed externally on the mother's abdomen at the fundus uteri, measuring changes in myometrial tension. Contractions can also be monitored internally with an IUPC, intrauterine pressure catheter, which measure the intrauterine pressure (19). External monitoring only gives accurate information about the frequency of contractions (90), whereas monitoring with an IUPC can increase the risk of fever of the mother (91).

CTG during labor

Stages of labor

Labor is divided into the first and second stage of labor. The first stage is the opening stage where the cervix dilates to ten centimeters. The second stage is the stage where the fetus moves down the birth canal pushed by contractions and active pushing. The first stage of labor is divided into a latent and an active phase. The definition of the start of the active phase of the first stage of labor was earlier an opening of the cervix of at least three cm and the start of the second stage was a fully dilated cervix (ten centimeters) (92). In 2018 the WHO decided on a new definition of the active phase of the first stage of labor to a cervix dilation of at least five centimeters. This definition was implemented in Sweden during 2022 (93, 94).

In the first stage the pressure on the fetus is less intense and in the second stage the fetus is affected both by the uterine contractions and by the active pushing. Thus, the CTG differs throughout labor and delivery. The higher pressure on the fetus in the second stage of labor makes this part the period with the highest risk for hypoxia of the fetus (95, 96).

Admittance CTG

Swedish guidelines state that it is useful to register an admittance CTG for risk evaluation when the laboring woman arrives to the delivery ward (31). The usefulness of admittance CTG is debated. A Cochrane review from 2017 found no benefit of admittance CTG in low-risk women on admission to labor wards and an increase in the CD rate. The review did not include enough data to evaluate perinatal death (97). A randomized Irish study from 2019 concluded that there were no differences in neonatal or obstetrical outcome with or without admittance CTG (98). It is conceivable that admittance CTG may not predict which labors that later will be complicated by fetal distress, yet CTG at admittance would be expected to identify those rare fetuses that are already exposed to hypoxia. To evaluate such a benefit, a randomized trial would have to be extensively large due to the rarity of these events.

During labor

If the admittance CTG is normal and the labor is classified as low risk, Swedish guidelines suggest intermittent auscultation or intermittent CTG during the opening stage with continuous risk evaluation. Intermittent CTG is as safe as continuous CTG in low risk labor (99). Continuous CTG is recommended if the labor is classified as high-risk or if the fetal heart rate is, or becomes, abnormal (31) , Figure 3. A continuous evaluation is needed of the CTG during labor.

Figure 3. CTG monitoring during labor
Intermittent CTG is recommended in the first stage of labor in low-risk labor and continuous CTG is recommended in high-risk labor. The tracing must be continuously evaluated.

A Cochrane review of CTG during labor concluded that the use of CTG increased the rate of CD without an effect on the rate of perinatal death (8) whereas Vintzileos et al found that surveillance with CTG was superior for fetal surveillance (7).

A recent review of fetal surveillance during labor found that intermittent auscultation is a safe method of surveillance. However, the included studies comparing CTG, and intermittent auscultation were old and of lower quality which may have affected the results (20). Since most of the studies comparing CTG with intermittent auscultation were carried out in a different clinical setting with one-to-one care and using different interpretation criteria (8, 19) their significance in modern practice may be doubted (19).

In the first stage of labor intermittent surveillance in low-risk pregnancy and continuous CTG in high-risk pregnancy are recommended (19, 31, 95). The duration of the registrations must be long enough for evaluation of the variables of the CTG (19). In the second stage of labor there is a higher risk of hypoxia. The contractions and the pushing of the mother adds higher pressure to the fetus, which may affect the fetal wellbeing (95, 96). The duration of the second stage is important for the risk of emerging fetal hypoxia (100). Continuous CTG may be recommended in the second stage of labor if the second stage of labor is prolonged (101). The protocol of the Swedish study evaluating intermittent CTG in low risk labor included continuous CTG in the second stage of labor, motivated by the more frequent occurrence of asphyxia in the second stage (99).

Maternal pulse

Surveillance of the maternal pulse

When monitoring the fetus with CTG the mother's pulse should be determined. Some CTG equipment can have a continuous surveillance of the mother's pulse. It can be either through an extra device or through the tocodynamometer (19). The monitoring of the maternal pulse is of extra importance if the mother has a health condition that needs surveillance or when the maternal and fetal pulse are hard to distinguish from each other (19).

Maternal pulse identified as fetal pulse

There is a risk of monitoring the maternal pulse instead of the fetal pulse, Figure 4. It is important to be sure who is monitored to get a safe fetal surveillance with safer classification of the tracings (102). If the maternal pulse is monitored instead of the fetal, there is a risk of major adverse neonatal outcome since the fetal heart rate is thought to be normal but is not even being supervised (103).

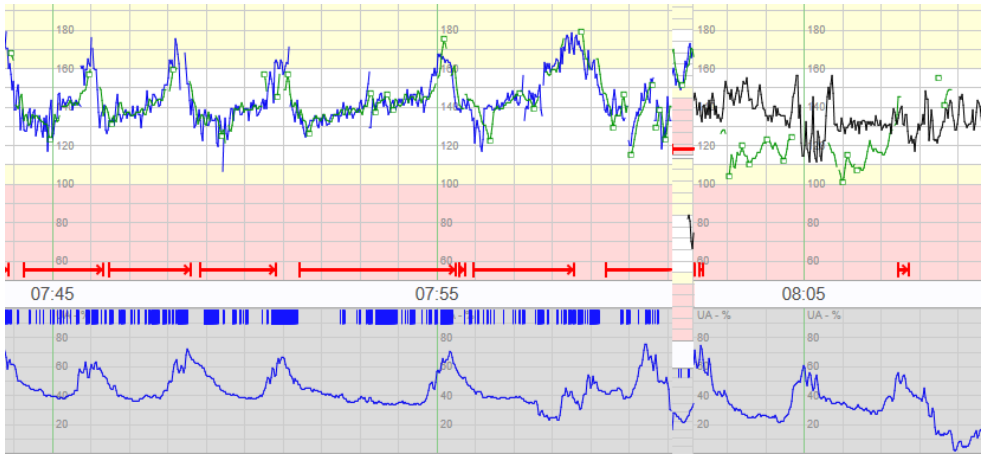


Figure 4. Maternal pulse
Maternal pulse registered as fetal. In the first part of the tracing the maternal pulse is registered as fetal. The green line is the maternal pulse registered with a pulse oxymeter.The fetus is not being supervised until the scalp electrode is applied.

In labor, especially in late labor, it is unusual for the fetus to react with an acceleration to a contraction. An acceleration at the same time as a contraction may be a sign of monitoring of the maternal pulse (78). A CTG with a low baseline, no decelerations in the second stage of labor and accelerations at the time of contractions are signs of recording of maternal pulse instead of fetal pulse (76, 77). It is more common with accelerations coinciding with contractions when using external monitoring of the fetus than internal, and it is important to know that it is the fetus that is monitored (75).

CTG guidelines

Overview

In 1987 the first international guideline of CTG was introduced by FIGO, FIGO87 (24). This was the first time they tried to find agreement on terminology, indication and interpretation of CTG. The guideline was spread and used in different forms in different countries but in some countries new guidelines were introduced (26). The ACOG, the American College of obstetricians and gynecology, has its own guidelines (47) as well as NICE (National Institute for Health and Care Excellence) (46) and the RCOG (the Royal College of Obstetricians and Gynaecologists) (104).The use of different guidelines was thought to be one of the reasons for it

being hard to prove the effectiveness of CTG (26). In Sweden the FIGO87 was used in an adapted form, SWE09 (27), similar to the STAN guideline from 2007 (28).

In 2015 FIGO introduced a new guideline for CTG. It was the first new international guideline since the FIGO87. The purpose was to have a guideline that is helpful both regarding the use and the interpretation of CTG (19) and having a guideline that is simpler and that has higher agreement (26). In Denmark and Norway they chose to keep their older guidelines, resembling the SWE09, since there was no robust evidence for a benefit in adapting to the new guidelines (32, 33, 34), whereas in Sweden it was chosen to adopt the guideline in an altered form, SWE17 (30).

Most guidelines use a three-tier system with categories normal, suspicious, and pathological. Others use a five-tier system classifying tracings in a five graded color scale (105, 106). When a three-tier system was compared to a five-tier system the former was found easier to use but the latter more helpful and having higher sensitivity (37, 107). A five-tier system has also been found to have the best balance between sensitivity and specificity (108).

FIGO guidelines from 2015

The FIGO15, Figure 5, was published by an international consensus panel of experts in CTG. It was presented in October 2015. The FIGO15 is a three-tier system, including normal, suspicious, and pathological (19).

	Normal	Suspicious	Pathological
Baseline	110 - 160 bpm	Lacking at least one characteristic of normality, but with no pathological features	< 100 bpm
Variability	5 - 25 bpm		Reduced variability for > 50 min, increased variability for > 30 min, or sinusoidal pattern for > 30 min
Decelerations	No repetitive decelerations		Repetitive late or prolonged decelerations during > 30 min. or 20 min if reduced variability, or 1 prolonged deceleration > 5 min
Interpretation	Fetus with no hypoxia/ acidosis	Fetus with a low probability of having hypoxia / acidosis	Fetus with a high probability of having hypoxia / acidosis
Clinical management	No intervention necessary to improve fetal oxygenation state	Action to correct reversible causes if identified, close monitoring or additional methods to evaluate fetal oxygenation	Immediate action to correct reversible causes, additional methods to evaluate fetal oxygenation, or if this is not possible expedite delivery. In acute situations immediate delivery should be accomplished

Figure 5. The FIGO15
The CTG guideline presented by FIGO in 2015, FIGO15.

The guideline was not evaluated before the introduction but has been after the introduction. Olofsson et al compared the FIGO15 with the SWE17 (30) and the STAN template from 2007 (28) and found that they classify tracings differently and that the FIGO15 had a lower sensitivity to identify acidemia than the STAN template from 2007 (35, 36). Martí Gamboa also found a low sensitivity for the FIGO15 (109). When compared to the NICE guidelines from 2007 and 2014 the FIGO15 was found to have better agreement scores and to be easy to use. It did not lead to a high range of interventions but the validity of the classification according to the template was not studied (38). A recent study compared the FIGO15 guideline to the ACOG guideline, the NICE guideline and the Chandraharan guideline. They found no statistical difference between the templates' diagnostic capacity (39).

Swedish guidelines

The SWE09

In Sweden a CTG interpretation template was introduced in 2009, SWE09, Figure 6. (27). It was a version of the FIGO87 (24) with modifications from the STAN template from 2007 (28). It was in use in Sweden between 2009 and 2017. The SWE09 was introduced through the Project Safe Delivery Care. It was a project were obstetricians, midwifes and neonatologists worked together with LÖF, the health care regions common insurance company, to improve safety in Swedish delivery care and included all delivery units in Sweden (27). Just as with the FIGO15 it was the result of a consensus panel and not evaluated before introduction.

CTG-klassificering	Basal hjärtfrekvens	Variabilitet / Accelerationer	Decelerationer	Kontraktioner
Normalt CTG	• 110-150 slag/min	• 5-25 slag/min • ≥2 accelerationer/60 min	• Inga decelerationer • Uniforma tidiga decelerationer • Variabla okomplicerade decelerationer med en duration <30 sek och amplitud <60 slag	• 5 eller färre kontraktioner/10 min
Avvikande CTG	• 100-110 slag/min • 150-170 slag/min • <100 slag/min i ≤3 min	• <5 slag/min >40 min utan accelerationer • >25 slag/min (saltatoriskt mönster) • <2 accelerationer/60 min	• Variabla okomplicerade decelerationer med duration 30-60 sek och/eller amplitud >60 slag	• >5 kontraktioner/10 min
	Vid en kombination av 2 eller fler avvikande faktorer klassificeras CTG-kurvan misstänkt patologisk			
Patologiskt CTG	• >170 slag/min • <100 slag/min i >3 min	• <5 slag/min i >60 min utan accelerationer • Sinusoidalt mönster	• Variabla komplicerade decelerationer med en duration >60 sek • Uniforma sena decelerationer • Kombinerade decelerationer	
Preterminalt CTG	• Upphävd variabilitet (<2 slag/min) utan accelerationer, oavsett decelerationer/hjärtfrekvens			

Figure 6. The SWE09
The Swedish CTG guideline from 2009

It was a four-tier system with categories normal, suspicious, pathological, and preterminal. If the tracing was classified as preterminal, delivery was an urgent need. A tracing classified as pathological needed further attendance whereas a suspicious tracing only needed continued surveillance. A normal tracing could be turned off if there were no other need for continuous surveillance.

SWE17

After the introduction of the FIGO15 a Swedish consensus panel consisting of obstetricians and midwifes introduced the SWE17, Figure 7 (30).

The SWE17 was a normalization and simplification of the older SWE09 guideline. The normal range of the baseline was widened to 110-160 bpm, the time periods for variability was changed, the demand of accelerations for classification normal was removed and repetitivity was introduced regarding all decelerations except for a prolonged deceleration of more than five minutes. Contractions were no longer a part of the template (30).

	Normalt	Avvikande	Patologiskt
Basalfrekvens	• 110-160 spm	• 100-109 spm • > 160 spm	• < 100 spm
Variabilitet	• 5-25 spm		• < 2 spm (upphävd)[a] • < 5 spm > 60 min[b] • > 25 spm > 30 min • Sinusoidalt > 30 min
Decelerationer	• Inga repetitiva[c] • Repetitiva[c] variabla okomplicerade / uniforma tidiga	• Repetitiva[c] variabla komplicerade med normal basalfrekvens och normal variabilitet	• Repetitiva[c] uniforma sena > 30 min; vid takykardi/nedsatt variabilitet > 20 min • Repetitiva[c] variabla komplicerade vid takykardi/nedsatt variabilitet > 20 min • Repetitiva[c] förlängda (> 3 min) • En förlängd (> 5 min)
Tolkning	• Ej pågående hypoxi	• Låg risk för hypoxi	• Medel/hög risk för hypoxi
Åtgärd	• Ingen åtgärd[d]	• Korrigera reversibla orsaker • Fortsatt CTG • Överväg stimuleringstest / skalpblodprov	• Korrigera reversibla orsaker • Utför stimuleringstest / skalpblodprov eller förlös

Figure 7. SWE17
The Swedish CTG guideline from 2017.

The template is a three-tier system with categories normal, suspicious, and pathological. If a tracing is classified as suspicious a FBS should be considered as well as correcting reversible causes for the tracing being suspicious. If a tracing is classified as pathological a FBS or delivery should be performed. This is in concordance with the FIGO15 (19, 30).

This guideline was not evaluated before introduction and implementation. After the introduction Olofsson et al found that the SWE17 classified CTG tracings differently than the STAN guidelines and the FIGO15 (36). After the implementation of the SWE17 a follow up study of two cohorts was performed. It was found that after the implementation of the SWE17 the rate of HIE grade II and III was insignificantly higher. The rates of neonates born with acidemia, and low Apgar scores were significantly higher after the implementation and the rate of operative deliveries was lower (110).

Agreement and CTG

Agreement, harmony in opinion, is used to measure the degree of accordance between two or more sets of interpretations (111). It is used to assess if the observers of for example a CTG tracing agree in their interpretation of the tracing.

Kappa index, κ, is used to compare agreement. According to McHugh a κ between 0 and 0.20 is none, 0.21-0.39 minimal, 0.40-0.59 weak, 0.60-0.79 moderate, 0.80-0.90 strong and above 0.90 almost perfect agreement (112).

CTG is a surveillance method with low agreement, both intra observer and inter observer (113, 114), where intra observer is agreement if the same assessor assesses a tracing twice and inter observer is when two different observers assess the same tracing. The classification terminal has high agreement whereas decelerations have low agreement (115). Low agreement may be one of the reasons why benefits of CTG have been hard to prove and was one of the reasons why FIGO presented a new guideline in 2015 (26).

When the FIGO15 was compared to a five-tier system (by Parer and Ikeda (105)), the five-tier system was found to have higher agreement in classifying a pathological tracing (109). Bhatia et al found that the FIGO15 had slightly higher agreement scores than the NICE guidelines. Their study did, however, not look at the outcome of the neonates, so the quality of the template was not considered (38).

The agreement scores for CTG are low and are not affected by the clinicians' experience or workplace (116). This is true for the FIGO15 as well. Rei et al found that κ for the classification of the tracings were 0.39 and that agreement did not differ with length of experience (117).

It is not only agreement on the classification of the tracing that is important. Ayres-de-Campos et al studied agreement of the FIGO87 guidelines and the clinical decision after using the guideline. They found an inconsistency in classification and clinical decision which they concluded could affect the outcome when going through cases that didn't go well (118). The same was concluded in a study of the interpretation of CTG by midwives. The agreement scores ranged from fair to good

and it was concluded that this could affect intrapartum care and the results of clinical audits (119).

It is also known that knowing the outcome of the neonate influences how a CTG is classified, and it also influences the agreement scores when assessing a tracing in retrospect (120, 121).

CTG Education

CTG is printed recordings of the fetal heart rate. There is a risk of misinterpretation due to human factors. It is important with education of CTG to improve knowledge of the fetal heart rate and the interpretation of the CTG, as well as to improve the quality of care (29, 104).

Education in Sweden

In Sweden all professionals working with CTG are obligated to train in CTG and to repeat the training. There is an online CTG training program that is fully available with education in CTG and with a test at the end (31). All Swedish residents in obstetrics and gynecology also have to attend an on-site course in CTG and fetal surveillance (122).

CTG education online

The most used CTG educational program in Sweden is the online training program, www.ctgutbildning.se (31). It was introduced during the Project Safe Delivery Care (27). When the SWE09 was in use in Sweden the program was based around the SWE09 interpretation template and during 2018 it was adapted to the SWE17. The purpose of the program is to ensure the competence of CTG in all midwives and physicians working with delivery care in Sweden since 98% of the malpractice during delivery care was due to deficient fetal surveillance (27). The program is held up to date by obstetricians and midwives and is financially supported by LÖF (31).

Benefits of CTG education

A review of 20 studies on CTG education, where nine were web based, found that CTG training was associated with improved safety and a reduction of unfavorable outcomes in obstetric care. The interpretation skills were higher after education and intrapartum management was improved (123). A French study found that an online training program improves the interpretation of CTG tracings (124) but a study of

the Swedish online education of CTG did not see improvements in the classifications of CTG tracings after going through the education program (125). Thellesen et al found that CTG education raised the knowledge of CTG but in a large study of cohorts, before and after the implementation of a national CTG educational program, they found no reduction of the incidence of hypoxia at birth after the implementation (126, 127).

A systematic review found that physicians with a longer career did not follow guidelines as well as younger physicians (128) and the interpretation skills of CTG are higher in the beginning of the career and lower after working for more than 15 years (127). Working in large units with many deliveries is associated with higher knowledge of CTG (127).

Secondary tools to cardiotocography

Since CTG is a method with a low positive predictive value, PPV, secondary tools are of importance. A low PPV may lead to unnecessary interventions. To reduce the rate of unnecessary interventions secondary tools to CTG have been developed (129).

Since the introduction of CTG the CD rate has increased and continues to increase (23). Although fetal distress is only one of many indications for CD. In Sweden about 14.5% of term CDs are performed on indication fetal distress, and about 2.4% of all term deliveries are CDs due to fetal distress (ref; the Swedish pregnancy Register 2018-2022). According to a Cochrane review the CD rate was higher with continuous CTG than with intermittent auscultation. They concluded that with continuous CTG there would be one extra CD per 11 monitored continuously with CTG during labor (8).

To improve the specificity of CTG, secondary tools are used to reduce the rate of unnecessary interventions. The secondary tools to CTG used currently is FBS, FSS, STAN and computerized analysis (129).

Fetal blood sampling

Fetal blood sampling, FBS, were described by Saling in 1962 (130). A small cut is made in the scalp of the fetus and a small amount of blood is collected and analyzed for pH or lactate. The membranes must be ruptured and the cervix must have started to dilate (129). The method can be used as a complement to CTG when the tracing is classified as suspicious or pathological (19). It cannot be used if the presenting part is uncertain, if the mother has an blood borne infection or if the fetus may have a coagulation disorder (129).

FBS measuring lactate is more likely to be successful than FBS measuring pH, due to the smaller amount of blood needed and is probably a more sensitive method (131, 132, 133). A Swedish RCT comparing pH and lactate analysis in FBS found no difference in neonatal outcome (133). A pH lower than 7.2 or a lactate above 4.8 mmol/L (measured by Lactate Pro 1™) are considered as indications for a need of an intervention (129, 132). The lactate cut-off, however, differs depending on what meter that is used (134, 135). With the StatstripXpress®, currently used at the delivery wards at Skåne University hospital, a cut-off of 5.2 mmol/L is considered as a safe cut-off to determine whether further intervention is needed (135).

A Cochrane review of CTG concluded that the use of FBS combined with CTG increases the rate of instrumental deliveries but decreases the rate of neonatal acidosis (8), but in an indirect comparison of RCTs comparing CTG with or without the option of FBS, the use of additional use of FBS seems to decrease the rate of instrumental delivery and lower the rate of neonatal acidosis (136). A Swedish study concluded that FBS is easy to use and tolerated by the patients (137). FBS is mostly used in northern and central Europe and not at all in the United States (129). It is not used in the United States because the use of CTG alone was said to be as safe for fetal surveillance (129, 138).

Fetal scalp stimulation

Fetal scalp stimulation, FSS, is the stimulation of the fetus scalp trying to provoke an acceleration. It can be used to differ between a sleeping fetus and a hypoxic fetus (129).

A meta-analysis concluded that FSS was safe to use when CTG was not reassuring to rule out acidemia (139) and it has been found to be useful when FBS is not available (140).

No reaction at FSS is associated with adverse neonatal outcomes and a FBS pH <7.20 (141, 142), but there is a risk of an acceleration even at a low pH (143). Studies have shown that an absent reaction from the fetus, no acceleration at stimulation, is a normal reaction in the second stage of labor and does not give more information than the CTG on its own (144, 145). A present reaction at stimuli may be a positive signal but no reaction, which is common, does not give more information than the CTG alone. Current Swedish guidelines state that a provoked acceleration after FSS rules out hypoxia just as safe as spontaneous accelerations (31).

STAN

The electrocardiogram, ECG, of the fetus may be altered by hypoxemia. It is the waveform of the ECG that is affected (146). STAN, ST-analysis of the fetal ECG, is a compliment of CTG to be used during delivery. It was developed in Sweden. It requires the use of a scalp electrode; therefore, ruptured membranes are required. It also requires continuous CTG surveillance and it is dependent on the knowledge of CTG interpretation (28).

Based on a Swedish RCT it was concluded that the use of STAN combined with CTG was better than CTG alone to identify hypoxia of the fetus and had higher agreement (147, 148, 149, 150), but even when using STAN it was important to act if the CTG alone was severely pathological or long lasting pathological (151). Later a large American randomized study found no differences in outcome between the groups with CTG alone or CTG in combination with STAN (152) and a meta-analysis and a Cochrane report both concluded that it was not justified to use STAN in obstetrics due to the modest benefits and disadvantages such as requiring continuous CTG and a scalp electrode (146, 153) There were no benefits seen in primary outcomes (CD rate and neonatal metabolic acidosis or encephalopathy), but in secondary outcomes. Fewer FBS and operative deliveries was seen with CTG combined with ECG analyzing (146).

Computerized CTG analysis

Antepartum surveillance with CTG may be combined with computer analysis to help the interpreting of the tracing. It may give an objective interpretation of the tracing, mainly of the variability (129). A low short term variability measured by a computer system can predict an unfavorable neonatal outcome (154). Changes in short term variability are difficult to identify visually, and a computerized interpretation is useful (155). The analysis of the antepartum CTG with computer must be according to the age of the fetus since the CTG changes with gestational age (41).

Intrapartum CTG in combination with computer systems has not yet been shown to be beneficial, but may be useful in the future (129). Systems used to help defining fetuses at higher risk for asphyxia may be useful. Fetal reserve index, FRI, is a system that may help the identifying of fetuses in the red zone, and this can be useful during intrapartum surveillance (156, 157). An RCT of computer analyzing of the CTG with built in alerts did not find maternal or neonatal benefits of this compared to visual interpretation of CTG (158). The INFANT trial, including more than 46.000 neonates, found no differences in outcome with computerized support of CTG interpretation and found that many of the abnormal CTGs were not identified by computer analysis (159, 160).

Drugs during labor

During labor the fetus may be exposed to drugs such as oxytocin, nitric oxide, epidural analgesia, and intravenous or oral opioids. Oxytocin is used for augmentation of labor and the other as analgesia for the mother.

Oxytocin stimulation

Endogenous oxytocin is a hormone that lowers stress levels and induce wellbeing of the human (161).

Prolonged labor is a risk for both the mother and the fetus and is a common cause for still birth in developing countries (162, 163). Uterine activity is increasing with oxytocin infusion, and the activity increases more with higher infusion rate (164).

Oxytocin should not be given routinely, only on a clear indication. If the contractions are thought to be insufficient and causing prolonged labor oxytocin is given intravenously as augmentation of labor. This can be done both in the active phase of the first stage of labor and in the second stage of labor. Women should not be left unattended, and proper surveillance of the mother and fetus is indicated (165, 166). There is a risk of hyperstimulation, with a risk of fetal distress, and therefore it is important to monitor the fetal heart rate and the contractions when oxytocin is given (165).

The use of oxytocin shortens the length of labor but does not increase the normal delivery rate (167). Oxytocin augmentation entails a risk of hyperstimulation that may affect the fetal heart rate and oxygenation (167, 168). The risk of tachysystole doubles when oxytocin is given and the hyperstimulation may affect the fetal heart rate and it increases neonatal morbidity (85). Incautiously use of oxytocin is seen in malpractice cases with fetal asphyxia (84) and is an important risk factor for acidemia at birth (169). In a case-control study, oxytocin administration was reported to be associated with an adjusted OR of 2.1 for acidemia at birth (170).

The oxytocin on its own does not affect the fetal heart or brain, and thus not the CTG of the fetus (171). A previous study found, however, that the oxytocin may influence the fetal heart rate by reducing the rate of accelerations after FBS (144). Holzmann et al found no correlation between oxytocin administration and reaction with acceleration by FBS (145).

Labor analgesia

Factors that affect the experience of labor are involvement, pain and support (172). Pain relief during labor is important and in Sweden a right for women in labor. Pain relief can be non-medical and medical. The most used medical analgesia in Sweden

during labor is nitrous oxide, opioids, and regional analgesia (spinal or epidural analgesia). In Sweden there is a consensus that it is the laboring women's need and personal choice that are most important in the choice of analgesia. Some of the analgesia may affect the fetus and the fetal heart rate (173).

Nitrous oxide

Nitrous oxide is analgesia in the form of a self-administered inhalation. It is an odorless and tasteless gas (174). It is commonly used in Sweden. The use differs in the western world, and it is uncommon as birth analgesia in the United States (175). It is effective in reducing pain intensity during labor (176). It is used as analgesia in all stages of labor. Nitrous oxide is reducing pain, but the pain is still present. It is also reducing anxiety. It is self-administered and has no serious side effects (175). It has a positive effect on the birth experience even if it may cause nausea, vomiting and drowsiness. Neonatal side-effects are not seen. Nitrous oxide is not as effective as regional analgesia but is safe for the women and fetuses (177, 178).

Opioids

Opioids are used as analgesia during labor, either orally or parenterally. Opioids provide pain relief, but many women report moderate or severe pain even after the administration of opioids. Opioids cause side effects such as nausea, vomiting and sedation (179). Opioids passes the placenta barrier and may affect the fetus (173). The neonates may be sedated at birth and require an antidote treatment and the opioid treatment may affect early neurological scores and early breast feeding (173, 179).

Opioids has an impact on fetal heart rate patterns (179) but the administration of opioids does not alter the presence of accelerations in the CTG tracing (180). In a case-control study, opioid administration (meperidine) was reported to be associated with a twofold risk for acidemia at birth (170).

Epidural analgesia

Epidural analgesia is the most effective pain relief during labor and is increasing the satisfaction of the experience of the delivery. It is a central nerve blockade using local anesthetics leading to reversible loss of pain. It is widely used (181, 182). In older studies there was an increase in instrumental deliveries after the use of epidural analgesia but in more recent studies this is not seen, probably due to more modern techniques of epidural analgesia. Side effects are reduced mobility and a risk of maternal fever and urinary retention (181).

Epidural analgesia does not affect the neonate's status at birth or the CTG pattern (181, 183, 184) even if the local anesthetics is combined with an opioid (183). Epidural analgesia may cause a maternal fall in blood pressure due to effects on the

central nervous system and the blood vessels of the mother (173). The hypotension of the mother may affect the fetus, but the epidural analgesia does not (184).

Fetal metabolism and Perinatal asphyxia

Fetal metabolism

The fetus is relying on the mother for oxygen and nutrition. The fetus is dependent on a functioning maternal respiration and circulation and exchange through the placenta for a sufficient supply of oxygen and nutrition and to eliminate waste products and carbon dioxide, CO_2 (82). Hypoxemia to some extent is part of normal delivery but in some fetuses, it will result in asphyxia. It depends on the duration of labor, the intensity of contractions and on what reserves the fetus has to begin with (82).

The fetus is dependent on glucose as energy substrate (185). When the oxygen supply is sufficient the fetus metabolizes glucose to energy, CO_2, and water. The CO_2 will be eliminated through the placenta and the mother's lungs if the system is functioning. If there is a problem on the fetal or maternal side the CO_2 is not eliminated in the way, that is needed (186). The fetus needs a functioning umbilical flow to eliminate CO_2. If the umbilical blood flow is disturbed by too intense contractions the fetus cannot dispose the CO_2. This leads to respiratory acidosis, a high concentration of H^+, a low pH, due to a high concentration of CO_2, through:

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

The higher concentration of CO_2 will push the equilibrium to the left and cause a higher concentration of H^+. If the blood flow over the umbilical cord is restored the CO_2 can be eliminated and the concentration of H^+ will fall (186).

If the supply of oxygen is insufficient glucose is metabolized to lactate and H^+ and a much smaller amount of energy. The insufficient supply of oxygen, thus results in an impaired energy production (82).

When the fetus oxygen supply is too low the production of energy will cause a lacto-acidosis due to the production of H^+ and lactate. Buffers, proteins and HCO_3^-, will attract the H^+, causing a lowering in base excess; this is metabolic acidosis. Since the decrease in oxygen supply through the placenta will fall at the same time as the elimination of CO_2 is lowered the acidosis due to oxygen deficiency will been seen at the same time as acidosis due to increase in CO_2 (186).

When the oxygen supply to the fetus is too low, the oxygen concentration in the fetal blood will fall, hypoxemia. The fetus will reduce its activity level and growth

will be restricted. Hypoxemia can last for days to weeks but the fetal defense mechanisms will be impaired (187).

If the oxygen saturation in the fetal blood gets too low, the tissues supply of oxygen is not high enough to ensure an aerobic metabolism. Hypoxia is when the oxygen level in the tissues are lower than the need of oxygen (187). The fetus redistributes the blood flow to essential body parts such as the central nervous system, heart, and adrenal glands, and the fetus increases its heart rate. Through these mechanisms the fetus can handle hypoxia for hours, depending on its condition at the start of hypoxia (187).

Asphyxia, meaning loss of pulse, is the last stage of lack of oxygen in the fetus. This is when the supply of oxygen is so low that it affects the central organs of the fetus leading to acidosis in the vital organs. The fetus can handle this situation for minutes and there is a urgent need to restore the oxygenation of the fetus, most often through delivery (187).

Metabolism during labor

During labor the oxygen supply of the fetus is affected by the contractions. The contractions lead to a repetitive decrease in the access of oxygen to the fetus. The contractions compress the fetus and the umbilical cord, as well as decreasing the blood flow through the uterine wall and placenta (82, 188).When the contractions reach a magnitude of 60-90 mmHg, no blood will pass the uterine wall. This is the power of a strong contraction (31). The contractions will not just affect the supply of the oxygen but the fetal oxygen saturation. The lowering in oxygen saturation will, if not restored between the contractions, lead to acidosis. It takes the fetus 90 seconds to regain full oxygen saturation after a strong contraction (83) and high frequency of contractions results in a desaturation of the fetal brain (189).

It is normal for fetal pH to fall in some extent during labor. pH is lower in the second stage and lactate increases during labor (190, 191, 192, 193). In the second stage the fetus is at a higher risk for hypoxia due to the higher intrauterine pressure. This affects the fetus and the CTG may look different than in the first stage of labor (95, 96). When the pushing of the mother is added, the pressure is even higher, affecting the oxygen supply of the fetus (187). If the second stage of labor increases in duration from 30 to 180 minutes the risk for neonatal acidemia is twelve times higher (100).

Blood gases of the new-born

When the neonate is born the blood gases of the neonate can be analyzed through blood drawn from the umbilical vein and artery. The blood needs to be drawn right after the neonate is born since the breathing of the neonate affects the result. The

umbilical cord does not have to be clamped before the drawing of blood. An arterial and a venous sample should be drawn for a complete analysis (31, 187). The arterial blood comes directly from the neonate, giving information on the neonate's status, whereas the venous blood originates from the placenta. The arterial blood thus has a lower concentration of oxygen and a higher concentration of CO_2 resulting in a lower pH in the artery (186). To ensure that the samples come from different vessels the pH must differ at least 0.02 (194). The analysis gives us information of the acid-base status of the neonate and can give us an objective measure of an eventual fetal asphyxia.

The pH tends to fall during the delivery (190, 191) and an ideal pH of a newborn is 7.26-7.30. A pH above 7.2 implies a healthy fetus but a pH of 7.15-7.19 is not associated to adverse outcome of the neonate. A normal pH at birth will exclude birth asphyxia as a reason for a clinically depressed neonate (195).

Perinatal asphyxia

The reason for having fetal surveillance during labor is to avoid asphyxia developing during labor. Even if perinatal asphyxia today is rare, for the neonate and the family of the neonate it can have tremendous effects. In Sweden during 2018-2020 1.2% of the neonates had pH less than 7.05 and a low BE, or a pH less than 7.00 (110). That means that more than 1000 neonates were born every year with such a degree of acidosis.

What cut-offs that should be used as indication of exposure to significant hypoxia is not clear and different studies use different cut-offs for acidemia. In neonates with a pH less than 7.10 there was a high risk for admittance to NICU (30%) and ventilator support (10%) (196). The risk for adverse neurological outcome of the neonate increases with a pH less than 7.10, but the risk is still low if the pH is above 7.0 (195). A pH below 7.0 has been associated with HIE, a need of resuscitation and intubation of the neonate, seizures of neonate, low Apgar scores, and death (197, 198). A pH value less than 7.05 has been suggested to be a useful threshold to identify neonates exposed to significant hypoxia during labor (199).

The cause of asphyxia can be an acute catastrophe (e.g., abruption), short but repeated (e.g., contractions) or a worsening of a chronic hypoxia (e.g., placental insufficiency). The fetus has defense mechanisms against hypoxia and when these are exhausted there is a narrow window between surviving without sequela and death (200). In asphyxia the fetus maintains cerebral blood flow by increasing its blood pressure but if the asphyxia continues the autoregulation of the blood pressure will be lost, causing hypotension and brain damage (201).

Hypoxic ischemic encephalopathy

Hypoxic ischemic encephalopathy, HIE, is neonatal encephalopathy caused by intrapartum asphyxia. HIE is graded according to the Sarnat classification in three grades, mild (I), moderate (II) and severe (III). The grading is based on an evaluation of the neonate's neurological status (202, 203). Metabolic acidosis, low Apgar scores at five and ten minutes and cerebral oedema in imaging, are required for the diagnosis of HIE (204). Mild HIE is distinguished by hyper alertness and irritability of the neonate and moderate HIE by a reduced level of consciousness, hypotonia and seizures. Moderate HIE has a 10-30% risk of death or cerebral palsy. Severe HIE, most often coma of the neonate, causes death or neurological sequela in most cases. With mild HIE most neonates are not affected in long term (204).

In Sweden 0.8 per 1000 neonates are diagnosed with HIE grade II or III (110). World-wide it is estimated that 8.5 per 1000 living neonates developed HIE. Of these, 96% were born in low- and middle-income countries. Access to obstetrical care and neonatal resuscitation could prevent many of the cases in low- and middle-income countries (205).

Beside systemic support of the neonate's cardiovascular and respiratory system, hypothermia is the main treatment of HIE (203). Treatment with hypothermia is effectful on the neurological outcome of the asphyxiated neonates. It is useful in term and near-term neonates with moderate and severe HIE. It reduces the mortality and long-term morbidity. The HIE must be diagnosed, and the treatment initiated, prior to 6 hours of age (206, 207). Hypothermia is a treatment that is effective in high-income countries but may not be that in low- and middle-income countries. Other treatments for preventing lasting impairment after HIE may be drugs such as erythropoietin and allopurinol. These drugs are now in trials to evaluate clinical usefulness. An option of hypothermia is a hope for neonates born outside high-income countries (208). After the acute event, the asphyxia, the injury in the brain evolves through the acute (latent), subacute (secondary) and chronic (tertiary) phases. Different therapies may be effectful in different phases. The hypothermic treatment is most effectful in the acute and subacute phase (209).

Only about 8-20% of cases with cerebral palsy are thought to be caused by intrapartum asphyxia (204, 210) and the rate of cerebral palsy has not decreased since the introduction of CTG (13).

Apgar score

Apgar score is a scoring system used to assess the wellbeing of the infant after birth. It was first proposed by Virginia Apgar in 1953. The newborn's wellbeing is assessed through five parameters, heart rate, respiration, muscle tone, irritability, and color (211). In each parameter the scores 0, 1 or 2 can be given, resulting in a

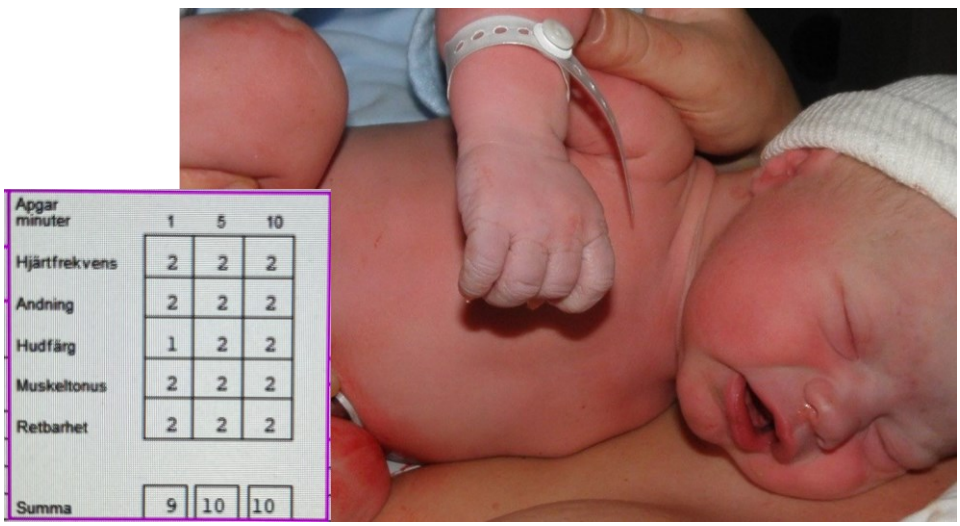
total score of 0 to 10 points. The scoring is at one, five and ten minutes, Table 1. It is as useful today for the predicting of the neonates survival (212).

Table 1. Apgar score
A scoring system to assess the wellbeing of the neonates

Score	0	1	2
Heart rate	Absent	<100 bpm	>100 bpm
Respiration	Absent	Slow, irregular	Good, strong cry
Muscle tone	Limp	Some flexing	Active motion
Irritability	Absent	Minimal response	Prompt response
Color	Blue, pale	Pink body, blue hands, or feet	All pink

Most vigorous newborns have an Apgar score of 9-10-10 since most newborns have a peripheral cyanotic color at one minute's age, Figure 8. If only the Apgar score is low at one minute it does not correlate to the neonate's outcome in the future (213), whereas a low (0-3) five-minute Apgar score is strongly associated to death (214).

A low Apgar score on its own does not diagnose asphyxia. The score is affected by other parameters such as gestational age, some medications given to the mother, and some anomalies of the fetus (215). However, in term infants without severe malformations most low five minute Apgar scores are due to asphyxia (216). In Sweden 0.5% of the newborns had a low five-minute Apgar score of 0-3 during 2017-2021 (217).



Fugure 8. Apgar score 9-10-10
A periferal blue tone of the hand in a vigorous newborn and the entry of the Apgar score in the mother's medical file.

Preventing asphyxia

The rate of moderate or severe HIE is low in Sweden (0.08%), still that means that almost 1000 neonates are affected each year. For the individual family it doesn't help that it is only 0.08% that are affected, they are affected to 100%. During 2021 LÖF paid about 100 million SEK due to obstetrical complains, related to childbirth, which is about 17% of their annual compensations to persons injured during healthcare (ref; personal communication with Pelle Gustafsson, Chief Medical Officer LÖF). A reason for the high expense is that the neonates are injured for life, at the very beginning of life (84).

Different fetuses have different possibilities to handle the delivery and how the labor progresses effect the fetus wellbeing. In his Masterclass of CTG (218), Edwin Chandraharan compares this with a marathon. A runner with a preexisting condition (such as intrauterine growth restriction, IUGR, of the fetus) is unable to withstand the stress of the marathon, they should not start. During the marathon a gradually evolving hypoxic stress affects all runners, this is normal, but even a healthy runner may be unable to handle an extra stress (oxytocin, prolonged length of the second stage of labor) for a longer period. Finally, all runners may encounter an unexpected event (abruption, cord prolapse) that will obstruct them from reaching the finish line. It is important that we consider this when assisting in deliveries.

Since different fetuses have different starting points, it is important to make a risk evaluation. In high-risk pregnancies continuous CTG during labor is recommended whereas it is not in low-risk pregnancies (38). When a CTG is started an evaluation of the situation should be made. A recommendation is to evaluate the baseline FHR (is it age appropriate), confirming presence of accelerations (usually present in early labor), exclude shallow late decelerations and to consider the whole clinical picture (High-risk? Signs of infection? IUGR? Meconium?) (40).

During labor intrapartum asphyxia can develop acutely (abruption, uterine rupture, cord prolapse) and rapid delivery is needed. Theses fetuses may have had normal CTGs before the event but often react with bradycardia at the acute event. If the asphyxia evolves gradually, the CTG is changed gradually, accelerations disappear, the base line increases, variability is lowered, and decelerations occur. If these signs are present, it is important to reduce the stress of the fetus by changing position, terminate oxytocin infusion, or taking a pause in pushing. If this doesn't help delivery may be needed (95).

Avoiding asphyxia is the main purpose of fetal surveillance during labor, and the goal is to identify emerging hypoxia that may precede to asphyxia, and thus avoiding asphyxia and fetal injury (19). By intervening at the right time birth asphyxia may be prevented and perinatal outcome improved (219). Still, since CTG has a low PPV, monitoring may cause unnecessary interventions. Therefore, it is important to use CTG correctly and to intervene at the right time. The use of CTG is only one part of clinical practice and not an excuse for leaving the mother alone during labor (19, 95).

Aims, specific aims

The general aim of this thesis was to evaluate the diagnostic performance of the CTG guidelines SWE09, FIGO15, and SWE17.

Paper I

To evaluate the sensitivity and specificity for the CTG interpretation guidelines SWE09, FIGO15, and SWE17, to detect acidemia after vaginal birth or CD in the second stage of labor.

Paper II

To evaluate the sensitivity and specificity for the CTG interpretation guidelines SWE09, FIGO15, and SWE17, to detect acidemia in the first stage of labor.

Paper III

To evaluate the presence of sporadic and periodic fetal heart rate accelerations and their association to acidemia at birth. To evaluate the association between fetal heart rate variability and the occurrence of accelerations to acidemia. To evaluate the association between other factors and the presence of sporadic accelerations in non-acidemic fetuses.

Paper IV

To evaluate the perceived need for intervention in cases with and without acidemia at birth after classifying the tracings using SWE09 and SWE17. To evaluate the sensitivity and specificity for the SWE09 and SWE17 to detect acidemia at birth, when used by two comparable groups of residents.

Materials and Methods

Use of CTG in the delivery wards

CTG is used as the main method of fetal surveillance at the delivery wards included in the study, the delivery wards at Skånes University Hospital in Malmö and Lund, and at the delivery ward at the Hospital in Helsingborg. At admittance to the delivery wards an admittance CTG is performed. If the admittance CTG is normal and the delivery is classified as low risk, intermittent CTG is recommended in the first stage of labor. If the admittance CTG is abnormal or the delivery is classified as high-risk, continuous CTG is recommended. Continuous CTG is generally recommended in the second stage of labor.

All midwives and physicians working in the delivery wards are obliged to do the online CTG educational program, www.ctgutbildning.se, (31) and to take the test regularly. In the delivery wards the SWE09 was in use prior to the implementation of the SWE17 in 2018.

The CTG tracings are stored electronically in the mothers' electronic medical files. The CTG surveillance software Milou™, Medexa diagnostic service AB, Malmö, Sweden, monitors and then archives the CTG tracings in the mothers' electronic medical files in Obstetrix™, Oracle Cerner, Austin, Texas, USA. The integration of the CTG tracings in the mothers' electronical files was completed in March 2012 in Helsingborg and in Malmö and Lund in April 2013. Therefore, the start of the inclusion period differs between the hospitals.

In all included delivery wards a paper speed of 1 cm/minute is used for CTG visualization.

Including neonates with acidemia

During the study period, April 23^{d}, 2013, to October 31st, 2017, at Skånes University Hospital in Malmö and Lund, and March 13th, 2012, to December 31st, 2016, at Helsingborg Hospital, 57.582 neonates were born. Of these 45.776 had available cord artery and/or vein samples. The neonates were identified through a search in the obstetric patients file system Obstetrix™. Only singleton pregnancies were included in the studies. The medical files of the mothers who had neonates with low

cord blood pH were scrutinized. If the CTG tracing fulfilled the inclusion criteria for Study I, or Study II they were selected and included in the study database.

Neither the FIGO15 guideline nor the SWE17 intrapartum CTG guidelines state that the guidelines are only valid from a specific gestational age (19, 30). However, the Swedish guidelines for antepartum CTG interpretation differ according to gestational week and the template for full term is valid from 34 weeks of gestation (31). Therefore, only deliveries after 34 full weeks were included in the studies.

Totally 295 neonates had a pH less than 7.05, were born in the second stage of labor (CD or vaginal), had an available CTG tracing for at least 30 minutes right before birth and were delivered after 34 weeks gestation. These 295 neonates were included in the study of the second stage of labor, Study I, as acidemic neonates.

Another 126 neonates were born with emergency CD in the active phase of the first stage of labor (three to nine cm dilation and regular contractions) and had an umbilical artery or vein pH less than 7.10. Of these 73 full filled the inclusion criteria for Study II: more than 34 weeks of gestation, available CTG of at least 15 minutes and with a shorter break than 30 minutes between the end of the CTG and the delivery. Inclusion criteria for all studies in the thesis are summarized in Table 2.

Adding controls

In both studies the neonates born consecutively after the included neonate with acidemia, at the same unit fulfilling the inclusion criteria were included. In Study I the two following neonates were included and in Study II the three following neonates were included. This was to raise power in Study II due to the low number of available neonates with low pH born in the first stage of labor with an available CTG.

Inclusion criteria were a gestational age of at least 34 weeks, Apgar score 9 or 10 at five and ten minutes and available pH from both artery and vein and at least 0.02 apart. This to ensure that the controls did not have a low umbilical blood pH, arterial or venous. In Study I, of the second stage, the controls had to have a pH $\geq$7.15 and in Study II a pH $\geq$7.20. For the non-acidemic groups the demands on the CTG tracings were the same as for the acidemic neonates in the two studies, at least 15 minutes for the first stage and at least 30 minutes in the second stage, Table 2.

The study numbers of the neonates with and without acidemia were randomized. Information about the neonate, the mother, and the delivery were gathered from Obstetrix.

Table 2. Inclusion criteria for the four studies included in the thesis
Inclusion criteria are diveded for neonates with and without acidemia and according to study.

	Inclusion criteria for cases with acidemia	Inclusion criteria for cases with normal pH
All studies	Births during 2012-2017 Singleton ≥34+0 gestational weeks In active labor	Births during 2012-2017 Singleton ≥34+0 gestational weeks In active labor Apgar score 9 or 10 at 5 and 10 min Delivered at the same site as the corresponding acidemic neonate
Study I	Delivered vaginally or with 2nd stage CD pH<7.05 in cord artery or vein ≥30 min of CTG ending at birth	Delivered vaginally or with 2nd stage CD pH≥7.15 in cord artery and vein and ≥0.02 apart ≥30 min of CTG ending at birth First two neonates fulfillng above criteria
Study II	Delivered by 1st stage CD pH<7.10 in cord artery or cord vein ≥15 min CTG ending <30 min from birth	pH≥7.20 in cord artery and vein and ≥0.02 apart ≥15 min CTG registered at the same cervical dilatation as the corresponding acidemic neonate First three neonates fulfillng above criteria
Study III	pH<7.05 in cord artery or vein after vaginal birth or 2nd stage CD or pH<7.10 after 1st stage CD ≥30 min CTG ending <30 min from birth	pH≥7.15 in cord artery and vein and ≥0.02 apart ≥30 min CTG registered at the same cervical dilatation as the corresponding acidemic neonate First two neonates fulfillng above criteria
Study IV	Cases from Study I and II assessed by residents Fulfilling criteria for Study I and II above	Non-acidemic neonates from Study I and II assessed by residents Fulfilling criteria for Study I and II above The first neonate fulfilling the above criteria

Gathering the CTG curves

All the included acidemic and non-acidemic neonates CTG tracings were saved from Obstetrix^{TM}. If the length of the last recording were longer than the demanded 15 and 30 minutes the whole available tracing was saved. The tracings exceeding 80 minutes were cut at 80 minutes, resulting in all included CTG tracings being 15 (30)-80 minutes long. All tracings had a paper speed of 1 cm/min.

The CTGs were saved as PDF files and given the same number as the included neonate. Figure 9. The tracings were saved on USB flash drives in groups of about 70.

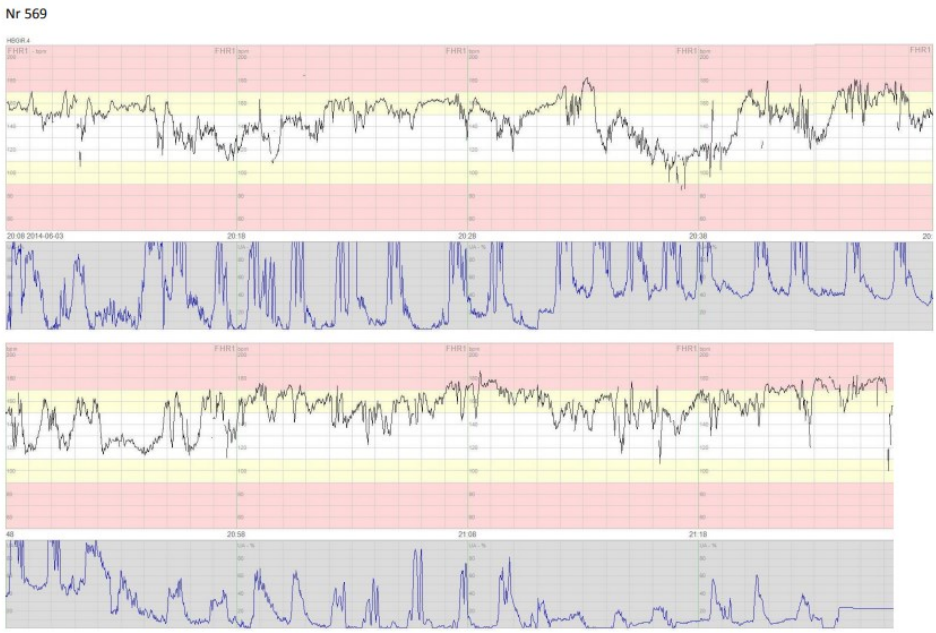


Figure 9. CTG tracing as assessed in the studies
The tracings were saved as PDF files and distributed to the assessors on USB flash drives.

Assessment of the CTG curves

The tracings were assessed by midwives and physicians (residents and obstetricians) working with CTG in their daily work at the included delivery wards. They had at least one year of experience and had all been through the online education on CTG. The tracings were assessed first, during 2017, using the SWE09 guidelines. During this period this was the only guideline in use in the delivery wards and the guideline that the education included. After the new guideline, SWE17, was introduced and everyone had worked with the SWE17 and had gone through the educational program with the SWE17, the CTG tracings were assessed again using the SWE17.

The assessors were given an USB flash drive with the tracings they were going to assess and printed templates to fill in. They were given information including that it was singleton pregnancies and if the tracings were from the first or second stage of labor. For the second stage tracings they were informed that all tracings ended with the birth of the neonate. They were not given any other information about the pregnancy, delivery, or the outcome. They filled in the guidelines, classified the tracings, and answered questions about for how long the classification had been present and if they wanted to intervene due to risk of hypoxia. An intervention was defined as a medical intervention, FBS or delivery.

Classification templates in the study

With the SWE09 the form used in the studies were the same as used in the clinic. The FIGO15 was fused into the SWE17 form since they are similar. The SWE17 was color-coded for the two forms, which enabled classification according to both forms. The forms as they were used are shown in Figure 10.

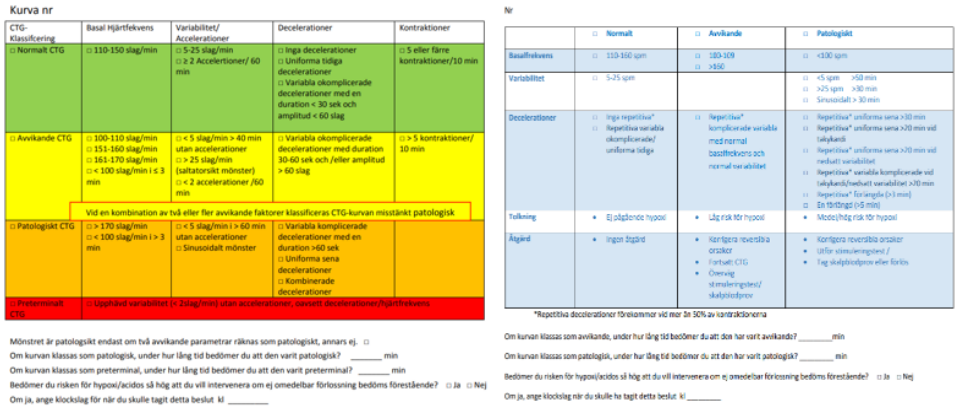


Figure 10. The forms used in Study 1.
The SWE09 and the combined SWE17 and FIGO15 as used in Study 1, where classification of the tracings and answering of questions were done. The forms were the same in Study 1 and 2, but the questions differed slightly.

Classification according to the guidelines

With all guidelines it was the classification according to the variables of the studied guideline that was used. If the assessors did not follow their assessment of the variables in their final classification, the final classification was adjusted according to the assessment of the variables. The classifications according to the guidelines were gathered in databases.

Each tracing was assessed by three assessors. If at least two out of three classified the tracing the same, this was the final classification. If all three classified the tracing differently a senior obstetrician made a fourth assessment and the classification that two of four agreed on was the final classification. In 118 of the total 1178 tracings interpreted with three guidelines, a total of 3534 interpretations, a fourth classification had to be made to reach a final classification. With SWE09 the fourth category, preterminal, was included in the category pathological in all calculations.

Paper I

Paper I is a retrospective study including neonates with and without acidemia, comparing the classification of their CTG tracings with three different classification guidelines. It was a study of the second stage of labor.

Cut-offs for asphyxia

In Study I the last part of the CTG tracings before birth in the second stage of labor were assessed. Totally 295 neonates born with acidemia were included. An arterial or venous cord umbilical pH <7.05 was considered as acidemia. The cut-off was chosen since this has been found to be a valuable cut-off for assessment of CTGs in the second stage of labor (199). This is a degree of acidosis that we certainly would want our monitoring to identify.

For controls neonates with an umbilical artery and vein pH ≥7.15 were included. A gap between acidemia and non-acidemia was wanted to get clearer groups. Inclusion criteria are shown in Table 2.

Sensitivity and specificity

The sensitivity for classification pathological (including preterminal with SWE09) to identify acidosis at birth was calculated as well as the specificity to rule out acidosis with classification normal or suspicious. With the SWE17 the interpretation suspicious may indicate the use of FBS for further evaluation of the fetal well-being. Therefore, a second analysis was performed where the sensitivity was calculated for classification pathological and suspicious in identifying acidosis and the specificity to rule out acidosis for classification normal.

Statistical methods

The sensitivity and specificity were calculated with 95% CI for the SWE09, FIGO15, and SWE17. The chi-square test was used to calculate the significance in differences between the three guidelines. A p-value less than 0.05 was considered statistically significant. The chi-square test was used since our focus was to compare differences between the classification systems within the two groups, i.e., neonates with and without acidemia. Proportions of agreement was calculated for the three templates.

Paper II

Paper II is a retrospective study comparing the classification of CTG tracings with three different classification templates from two groups of neonates, with and without acidemia. All CTG tracings were from the active phase of the first stage of labor.

Matching according to cervical dilation

In Study II CTG tracings from the active phase of the first stage of labor was studied. It was defined as a cervical dilation of three to nine cm and regular contractions since this was the definition of the active phase of the first stage of labor during the study period. CTGs from neonates born with acidemia in the first stage of labor were included. Since the CTGs differ in different stages of delivery the non-acidemic neonates' CTGs were matched according to cervical dilation. The CTG tracing from the acidemic neonate right before birth was matched with CTG tracings from the same cervical dilation in the non-acidemic neonates.

Since the recommendation in the included delivery wards is surveillance with intermittent CTG during the opening stage in low-risk deliveries, the available tracings were shorter. Therefore, tracings of shorter duration were included than in the study of the second stage of labor. The range in both acidemic and non-acidemic neonates were 16-80 minutes. The median duration of the tracings was shorter in the non-acidemic group than in the acidemic group, 40 minutes, and 70 minutes respectively. In the non-acidemic group 31% of the tracings were shorter than 30 minutes. In the acidemic group it was 8%.

Cut-offs for asphyxia

In Study II the cut-off for asphyxia was set at pH<7.10. The pH of the fetus normally declines during delivery (191, 192, 193) and therefore a higher cut-off than in Study I was used. A pH <7.10 is associated with adverse neurological outcome (195). The cut-off for non-acidemic neonates was set at pH ≥7.2. Only 126 of the neonates (8.6%) born with a pH <7.10 during the study period were born with CD in the first stage of labor. Of these 73 fulfilled the inclusion criteria and was included in the study. Inclusion criteria are summarized in Table 2.

Sensitivity and specificity

In Study II the sensitivity for identifying acidosis with classification pathological was calculated and the specificity for ruling out acidosis with classification normal or suspicious.

Statistical methods

Sensitivity and specificity with 95% CI were calculated. To determine the statistical significance between the sensitivity and specificity with the different templates a two-sided McNemar's test was used, with a $p<0.05$ being considered as statistically significant. The McNemar's test was used since the classifications of the same traces with different classification templates by the assessors were considered as matched.

Since there were three possible classifications of each tracing a free-marginal kappa (according to J Randolph, www.justusrandolph.net/kappa) was used to calculate agreement. For classification of the agreement index, McHugh (112) was used.

Paper III

This was a case-control study comparing the occurrence of accelerations and the variability in CTG tracings from cases with acidemia at birth and controls without acidemia at birth.

Compiling Study 1 and 2

The CTG tracings from Paper I and Paper II were compiled in this study. The cut-offs for acidemia were kept as in the original papers. For neonates born in the second stage of labor a cord arterial or venous pH <7.05 was regarded as acidemia and for neonates born in the first stage of labor a pH <7.10 was regarded as acidemia. The reason for the different cut-offs were the same as in Paper I and II, the falling in pH during labor (190, 191, 192, 193).

In Paper I the minimum duration of the tracings was 30 minutes and in Paper II it was 15 minutes. When merging the databases together all tracings shorter than 30 minutes was removed for uniformity. Thus 70 cases from Paper II and all cases from Paper I (295) was included, a total of 365 cases. If tracings included were longer than 60 minutes, only the last 60 minutes were studied in Study III. Thus, the studied tracings were all 30 to 60 minutes. Inclusion criteria are summarized in Table 2.

Adding new controls

In Paper I two non-acidemic neonates were included for each neonate with acidemia and in Paper II three. In Study III the two consecutively born neonates fulfilling the criteria for controls were used. Since the cut-off for non-acidemic neonates differed in Paper I and II, a uniform cut-off level was set in Study III to a cord arterial and venous pH ≥7.15 and at least 0.02 apart in Study III. After excluding CTG tracings shorter than 30 minutes and lowering the cut-off for non-acidemia in the neonates

from Paper II, 33 new non-acidemic neonates replaced the excluded ones. All non-acidemic neonates from Paper I were included in Study III and a total of 140 non-acidemic neonates born in the first stage of labor, leaving a total of 731 neonates born without acidemia. In total 1096 CTG tracings were included in Study III.

Assessment of accelerations and variability

In Paper I and II the assessors had assessed whether accelerations were present or not when using the SWE09. However, this template included all accelerations and did not differ between sporadic and periodic accelerations. All 1096 CTG tracings were therefore reassessed by the first author, to ensure the correct classification of accelerations. The definition of an acceleration was a rise of at least 15 bpm lasting for at least 15 seconds (19) and they were divided into sporadic and periodic according to Krebs (62), Figure 2. In uncertain tracings a co-author also defined the accelerations and the two authors agreed on classification. The tracings were divided into three groups: two or more sporadic accelerations (group one), two or more periodic acceleration but less than two sporadic accelerations (group two), or less than two of either kind of accelerations (group three), Figure 11.

The variability was assessed in Paper I and II by three assessors and the variability they agreed on was used in Study III. A variability of 5-25 bpm was considered as normal in concordance to guidelines (19, 27, 30). Reduced variability was divided in reduced (2-4 bpm) and absent (less than 2 bpm) in concordance with Swedish guidelines (27, 30). An increased variability was set at a variability of more than 25 bpm for at least 30 minutes according to the SWE17 and FIGO15 (19, 30).

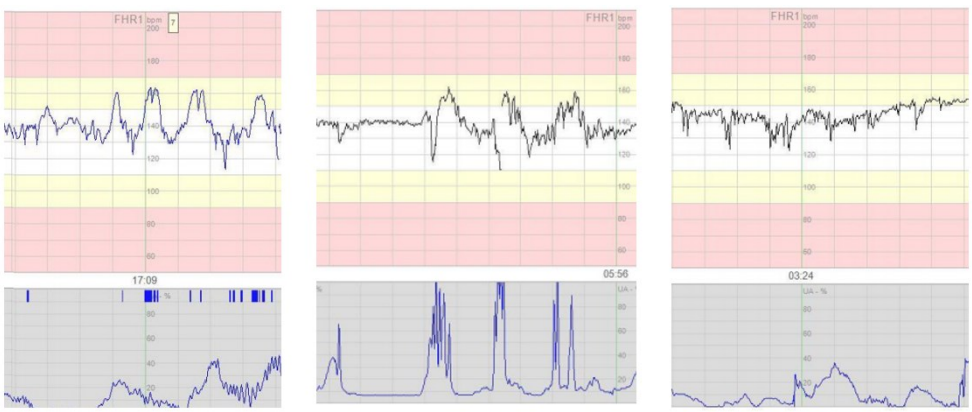


Figure 11. The groups of accelerations in Study III.
Sporadic accelerations, periodic accelertions and no accelerations present.

Maternal pulse

When assessing the tracings for accelerations periods within some tracings with maternal pulse were identified, Figure 12.

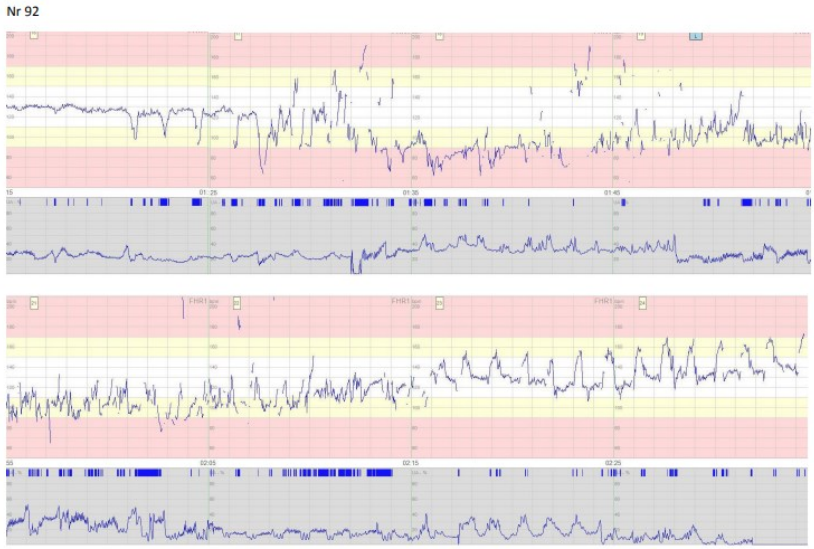


Figure 12. Example of a CTG tracing with maternal pulse and fetal pulse.
The last 19 minutes were excluded due to maternal and not fetal pulse. Therefore, assessment regarding accelerations was only done for the 41 minutes preeceding the part with maternal pulse (since only the last 60 minutes were included in the study). This tracing was in group 3, no accelerations present.

Maternal pulse was defined according to previous studies (75, 76, 77, 78, 102). In 14 tracings (11 cases and three controls) sequences of maternal pulse were found. A second author also scrutinized the tracings in which the first author had identified periods of registered maternal pulse confirming the interpretation. In all but one, it was a shorter period, and the tracing could be assessed just using the tracing including fetal pulse, but one tracing (from an acidemic neonate) had to be excluded due to including mostly maternal pulse. Thus, 1095 CTG tracings were finally included in Study III.

Statistical methods

OR with 95% CI was calculated for acidemia in the presence vs absence of accelerations. Sub-analyses were done for the first and the second stage of labor and for those with 60 minutes of registered CTG. OR for acidemia with different patterns of variability with and without sporadic accelerations present was also calculated.

To find out if other factors than acidosis may influence the presence of accelerations a regression analysis was done including other intrapartum factors in non-acidemic neonates: cervical dilation, analgesia, oxytocin, membrane rupture and monitoring with scalp electrode or external monitoring.

Paper IV

The intention to intervene and the classification of CTG tracings, from acidemic and non-acidemic neonates, were compared after assessments made by residents educated in and using either SWE09 or SWE17. The groups of residents had comparable education and clinical experience.

New assessors

In Paper I and II the tracings were assessed by midwives and physicians with differing length of experience. Even if they were all educated with the SWE17 prior to assessing the tracings with the SWE17 some had had a long experience using the SWE09 prior to the change to SWE17, which may have influenced their assessment.

Choosing residents as assessors

To get two comparable groups of assessors, that were not influenced by using both the studied templates, residents having only experience of one of the templates were chosen. In Paper I and II, ten residents assessed tracings using the SWE09. They had between one and four years of experience. They had been educated in and had clinical experience with the SWE09 and had not been using any other template in their daily work when assessing the tracings in the studies.

For Study IV a comparable group of residents was recruited. Ten new residents with one to four years of experience were chosen. Since the new assessment was done during 2022 none of the residents had been working in the delivery wards when the SWE09 was in use. They had had all their education and clinical experience with the SWE17. This made the two assessing groups comparable regarding experience and education. The online educational program (31) was the same for both groups (adjusted with template in use) and they had had the same on site course in fetal surveillance (122).

Choosing cases and controls

223 acidemic neonates CTG tracings had been assessed by residents in Paper I and II. These were included in Study IV. The inclusion criteria were therefore the same as in Paper I and II. As controls 223 tracings were included. They were matched for

cervical dilation and were all part of Paper I and II. A total of 446 tracings were included. Of these 86 tracings were from the first stage of labor and 360 from the second stage of labor. See Table 2 for inclusion criteria.

The assessment was completed in the same way as in Paper I and II. The assessors were blinded to outcome and had to fill in templates on paper and had the tracings on USB flash drives. They had to answer whether they had an intention to intervene due to risk of acidosis. An intervention was a FBS or delivery, a medical intervention.

Sensitivity and specificity

Sensitivity and specificity for perceived intention to intervene were calculated for both templates. The assessors had answered the question "Do you consider the risk for hypoxia/acidosis high enough that you would want to intervene?" with a yes or no. Sensitivity and specificity were calculated according to the answers.

Regarding sensitivity and specificity for classification the calculations were done in one way with SWE09, where pathological (including preterminal) were regarded as a positive test and normal and suspicious as a negative test. With the SWE17 the calculations were done in two ways. The same as with SWE09 and with pathological and suspicious regarded as a positive test and normal as a negative test. It was done this way since the SWE17 state that a FBS should be considered if the tracing is classified as suspicious. In this way, the sensitivity for perceived need for intervention and sensitivity for classification according to the template could be compared.

Agreement was calculated both for perceived need for intervention with the two templates, for classification with the two templates and comparing the classification and perceived need for intervention within the different templates.

Statistical methods

The sensitivity and specificity with the two templates both for classification and perceived need for intervention were calculated with 95% CI. In Study IV the interpretations were considered as matched and the McNemar's test to determine statistical significance was used. For agreement both between and within templates, both overall agreement in percent and Kappa index, κ, was determined.

Methodological considerations

Paper I and Paper II

Asphyxia during labor is a rare event. In Sweden during 2018-2020 1.2% of the neonates had pH less than 7.05 and a low BE or a pH less than 7.00 (110). A total of 572 neonates (1.0%), of the 57.582 neonates born at the included hospitals during the inclusion period, were born with a pH less than 7.05. A total of 368 fulfilled the inclusion criteria for acidemic neonates in the two studies. The ratios between acidemic/non-acidemic neonates in the studies were one to two and one to three. This is not at all as in real life where it would be closer to one to 100. This may have affected the assessors and the results. If enough acidemic neonates' CTG tracings should be included and we still would want the real-life ratio between acidemic and non-acidemic neonates, the amount of included tracings would be too large to enable a thoroughly study of the tracings.

The PPV and NPV of CTG are affected by the rareness of asphyxia. In the studies we could not calculate the PPV and NPV since the study groups were selected according to pH and not cohorts. This may be considered as a weakness of the studies. On the other hand, due to the low rate of acidosis, a cohort study would not be able to assess estimates of sensitivity with sufficiently narrow confidence intervals unless studying a very large cohort such as the complete cohort from which the study groups were selected.

All the included CTGs are from 2012-2017. During this period the SWE09 was in use in all the included delivery wards. It was the SWE09 that was used for CTG interpretation during labor and delivery of the included cases. This may have biased the estimates of sensitivity of the CTG templates in a negative direction, especially for SWE09, since cases with impending asphyxia not detected by CTG monitoring (using the SWE09 guidelines) would be more likely to be born with acidosis. It may also have biased the specificity of the CTG templates in a negative direction, especially for SWE09, since interventions in cases with pathological heart rate patterns may have obscured that some of these neonates born with normal pH may would have become acidemic without a performed intervention. It is therefore plausible that the true sensitivity and specificity of the studied templates may be higher than our estimates. Since it is not ethically to perform a blinded study of CTG today all studies of CTG will be influenced by the template that is in use at the time of the recording. Another way to compare the efficiency of different guidelines to prevent asphyxia is to study two different cohorts, one from where the SWE09 was

in use and one from where the SWE17 is in use. This was done in a Swedish study (110). Two cohorts from two different periods have other considerations however, the two cohorts will not be identical and much more than just the CTG guidelines have changed over the years. However, the results from the cohort study implied the same results as Paper I and Paper II.

Some of the assessors had worked in the delivery wards during the time when the SWE09 was in use. They were more used to this template. All had been working with the new template and gone through the educational program before the assessment with the SWE17. However, some were still more used to the SWE09 that had been in use for a longer period. This will always be the case when a new method is introduced and is hard to avoid. Paper IV, with just residents as assessors was an attempt to avoid this bias.

In clinical practice CTG is just one of the tools used during labor. In the studies the assessors did not get any clinical information except that it was singleton pregnancies, what stage the CTGs where from, that the second stage tracings all ended with delivery and that the tracings were either from acidemic neonates or from non-acidemic neonates. This design was chosen due to the knowledge that knowing the outcome of the neonate influences the interpretation of CTG tracings (120, 121). Since the same information was given to all interpreters, regardless of what template they used, this would affect the interpretation with all templates the same way.

In Paper I the chi-square test was used to calculate the significance in differences between the three guidelines and in Paper II the McNemar's test. The studies had similar design and therefore the same statistical method would have been appropriate for both studies. At first the chi-square was used in both studies. After the submission of Paper I, the question arose whether the studies should be considered as case control studies of neonates with and without acidemia (non-matched, using the chi-square) or as a study of the classification of the same tracings with different templates (matched, since the same tracing was classified, requiring the McNemar's test). It was decided that the second way was more correct why Paper II was recalculated with the McNemar's test, and it was also later used in Paper IV. Both studies were calculated in both ways for reassuring, and it gave about the same p-values. The significance of the results was not affected by the choice of statistical test.

The pH cut-offs for acidemia differed in the two studies due to the decline in pH and rise in lactate during normal delivery (190, 191, 192, 193). The cut-off for non-acidemic neonates differed as well in the two studies. The reason for this was that a gap between non-acidemic and acidemic neonates was wanted. However, the same cut-off for non-acidemic neonates in both studies might have been more logical since most of the non-acidemic neonates even in Paper II were born after a second

stage of labor even if the assessed CTG tracings were from the first stage. Because of this the cut-off in Paper III was uniformed to the cut-off in Paper I.

After scrutinizing the tracings for maternal pulse for Paper III, one tracing was excluded due to including mainly maternal pulse. This tracing should have been excluded even in Paper I but wasn't observed at the time. Attention for maternal pulse is not a part of either of the included templates and according to the templates the tracing was classified as normal with all three. This lowers the sensitivity for all three templates since the included tracing was from an acidemic neonate. This is something that needs to be considered in clinical practice. If the maternal pulse is traced instead of the fetal, the tracing may be classified as normal even if the fetus is at risk for asphyxia.

Paper III

In Paper III accelerations and variability was assessed. One person classified all the tracings regarding accelerations. If there were uncertainties one more person assessed the tracings for accelerations. If both had assessed all tracings the influence of one person's judgement in the result would be lower.

The tracings were scrutinized for maternal pulse. This was done by one person. In 14 tracings maternal pulse were found. These 14 tracings were also scrutinized by a second author for confirmation. But all included tracings were not assessed for maternal pulse by two authors so the first assessment regarding maternal pulse is the judgement of one person. This might entail a risk of subjectivity. Would two be better? Should the whole tracing have been excluded? One tracing was mostly containing maternal pulse and was excluded. The other 13 were assessed based on the parts with fetal heart rate recorded.

Paper IV

In Paper IV an attempt was made to avoid the bias that some of the interpreters in Paper I and II were more used to the SWE09. Residents who had only worked under the period that the template they assessed with in the study were in use, were chosen as interpreters. Still, the senior obstetricians that taught them about CTG in clinical practice, were still influenced by the old template and this might especially have affected the residents perceived intention to intervene.

Residents are under training. They are still more prone to adapt to and follow guidelines (128) and have high knowledge in CTG (127). The result of Paper IV may therefore not be applicable on other interpreters of CTG in our delivery wards. It would be interesting to perform the same study for more experienced users of CTG and for both midwives and obstetricians. Since they on the other hand would be more influenced by the SWE09 this was not the chosen approach in Paper IV.

With the SWE09 a tracing classified as suspicious was not considered needing an intervention, more than continued surveillance. With the SWE17 a tracing classified

as suspicious may lead to an intervention such as an FBS. Since the templates have different guidelines on how to act in the clinic, they can't be compared directly regarding intention to intervene. Therefore, the calculations regarding sensitivity and specificity were done for pathological and suspicious combined and for pathological alone with the SWE17 but only for classification pathological with the SWE09.

Ethical considerations

Ethical approval for the project and all the included Papers, was obtained from the Regional Ethical Review Board in Lund, Dnr 2016/371, 2016-05-24.

According to the ethical approval the mothers from who's deliveries the CTG tracing originated were not contacted. They have not been given the chance of saying no to be included in the studies. The ethics board approved this since it was retrospective studies only presenting data on group level and none of the included participants could be identified. However, all their journals have been scrutinized for information about their delivery and their neonate, and the information has been stored, pseudonymized, in a database.

When we applied for an extended ethical permission to include the period after the period included in this project, for access to more CTG tracings, the board demanded that all the persons that will be included in future studies have to be informed about the studies by letter and be given the chance to opt out from future studies. In one aspect, it may be more ethical to have the option not to be included in a study of the association between fetal heart rates patterns and acidosis at birth. On the other hand, contacting patients long time after having given birth, especially women having given birth to neonates with acidosis, might evoke worry, and in most cases unwarranted concern, about the wellbeing of their child.

Results and Comments

Paper I and Paper II

Results

In Paper I and II CTG tracings from neonates with and without acidemia were interpreted by midwives and physicians. The CTG tracings were from all acidemic neonates born in the first and second stage of labor, that fulfilled the inclusion criteria during the study period, and from the same cervical dilation from neonates without acidemia. Background data are presented in Table 3.

Table 3. Background data for included pregnancies.
Acidemic neonates are presented for first and second stage separately whereas non-acidemic neonates are presented for both studies combined.

	Acidemic Neonates First stage n (%)	Acidemic Neonates Second stage n (%)	Non-acidemic neonates n (%)
Total	**73**	**295**	**810**
Primiparous	34 (46.6)	190 (64.4)	384 (47.4)
Preterm birth 34+0 ≥36+6	0 (0)	8 (2.7)	21 (2.6)
Post-term birth ≥42+0	8 (11.0)	21 (7.1)	56 (6.9)
Birthweight < 2.5 kg	3 (4.1)	3 (1.0)	10 (1.2)
Birthweight > 4.5 kg	2 (2.7)	10 (3.4)	20 (2.5)
Breech	0 (0)	2 (0.7)	1 (0.1)
Fever/infection	6 (8.2)	5 (1.7)	11 (1.4)
Meconium-stained amniotic fluid	32 (43.8)	65 (22.0)	154 (19.0)
Diabetes	8 (11.0)	14 (4.7)	23 (2.8)
Preeclampsia	6 (8.2)	10 (3.4)	17 (2.1)
Body mass index <25 kg/m2	30 (41.0)	181 (61.4)	482 (59.5)
Body mass index >30 kg/m2	19 (26.0)	30 (10.1)	86 (10.6)
Smoking	5 (6.8)	17 (5.8)	59 (7.3)
Female fetus	26 (35.6)	133 (45.1)	413 (51.0)

The group of acidemic neonates born in the first stage of labor included more high-risk pregnancy than the non-acidemic group, whereas the group of acidemic

neonates born in the second stage of labor did not. There were more primiparous women in the acidemic group in the second stage of labor (64%) than in the group of acidemic neonates in the first stage of labor (47%) and in the group of non-acidemic neonates (47%).

All tracings, from both the first and second stage of labor got a final classification according to the three templates and those classifications are summarized in Table 4.

Table 4. Summary of classification according to the three templates.
Classifications are presented for first and second stage separately.

	SWE09 First stage n (%)	SWE17 First stage n (%)	FIGO15 First stage n (%)	SWE09 Second stage n (%)	SWE17 Second stage n (%)	FIGO15 Second stage n (%)
Acidemic	**73**	**73**	**73**	**295**	**295**	**295**
Normal	0 (0)	7 (9.6)	1 (1.4)	7 (2.4)	49 (16.6)	10 (3.4)
Suspicious	4 (5.5)	10 (13.7)	20 (27.4)	31 (10.5)	63 (21.4)	137 (46.4)
Pathological	69 (94.5)	56 (76.7)	52 (71.2)	257 (87.1)	183 (62.0)	148 (50.2)
Of which preterminal	*19 (26.0)*			*33(11.2)*		
Non-acidemic	**219**	**219**	**219**	**591**	**591**	**591**
Normal	166 (75.8)	204 (93.2)	165 (75.3)	167 (28.3)	400 (67.7)	133 (22.5)
Suspicious	31 (14.2)	8 (3.7)	47 (21.5)	161 (27.2)	101 (17.1)	384 (65.0)
Pathological	22 (10.0)	7 (3.2)	7 (3.2)	263 (44.5)	90 (15.2)	74 (12.5)
Of which preterminal	*1(0.5)*			*3 (0.5)*		

The three templates classified the CTG tracings differently. The FIGO15 gave a high proportion of tracings classified as suspicious, both in acidemic and non-acidemic neonates. The SWE17 gave a higher proportion of normally classified tracings than the other templates and with the SWE09 more tracings got classified as pathological. This applied in the first as well as in the second stage of labor.

Sensitivity and specificity were calculated for the three templates and are summarized in Table 5. With the SWE09 a suspicious tracing stipulated continuous surveillance whereas with the SWE17 and the FIGO15 it suggests an FBS. Therefore, sensitivity and specificity were calculated both for classification pathological vs suspicious and normal and for classification pathological and suspicious vs normal. Preterminal was included in pathological in all calculations. In the study of the first stage of labor (Paper II) the analysis of pathological and suspicious combined is not included in the published paper.

Table 5. Sensitivity and specificty according to templates with 95% CI.
Sensitivty and specificity are calculated separately for the first and second stage of labor and for both classification pathological and for classifications pathological and suspicious combined. For p-values see original articles and text.

	Sensitivity Classification pathological % (95% CI)	Specificity Classification pathological % (95% CI)	Sensitivity Classification pathological and suspicious % (95% CI)	Specificity Classification pathological and suspicious % (95% CI)
SWE09[1] First stage	94.5 (86.6-98.5)	90.0 (85.2-93.6)	100 (95.1-100)	75.8 (69.6-81.3)
FIGO15 First stage	71.2 (59.4-81.2)	96.8 (93.5-98.7)	98.6 (91.6-100)	75.3 (69.1-80.9)
SWE17 First stage	76.7 (65.4-85.8)	96.8 (93.5-98.7)	90.4 (81.2-96.1)	93.2 (89.0-96.1)
SWE09[1] Second stage	87.1 (82.8-90.7)	55.5 (51.4-59.6)	97.6 (95.2-99.0)	28.3 (24.7-32.1)
FIGO15 Second stage	50.2 (44.3-56.0)	87.5 (84.5-90.0)	96.6 (93.9-98.4)	22.5 (19.2-26.1)
SWE17 Second stage	62.0 (56.2-67.6)	84.8 (81.6-87.6)	83.4 (78.6-87.5)	67.7 (63.5-71.4)

[1] Including patterns classified as preterminal.

The sensitivity was higher with SWE09 in both the first ($p>0.001$) and second stage ($p>0.01$) of labor for classification pathological than with the other two templates, but the specificity was lower in the second stage of labor ($p>0.01$). If combining pathological and suspicious, the sensitivities increased for all templates and the specificities decreased. With the SWE09 and the FIGO15 the specificities decreased to very low levels. The sensitivity for classification pathological with SWE09 in the second stage of labor and for classification pathological and suspicious combined with SWE17 did not differ significantly ($p=0.20$).

The agreement was higher in acidemic neonates with the SWE09 in both the first and second stage of labor, but lower in non-acidemic neonates than with the two other templates.

Comments

When combing the results from Paper I and Paper II it was found that during the first stage of labor there were more high-risk pregnancies in the group of acidemic neonates, whereas in the second stage of labor this was not as obvious. For some neonates at risk the first stage of labor is enough for developing acidemia. In the group of acidemic neonates in the second stage of labor, there were more primiparous women, but there were no differences in high and low risk deliveries in other aspects. Neonates from low-risk pregnancies were at risk for acidemia as well as those from high-risk pregnancies. This strengthens the recommendations that in the first stage of labor high-risk pregnancies should be under continuous

surveillance and in the second stage of labor both high-risk and low-risk deliveries may be under continuous surveillance, especially if the second stage of labor is prolonged (101) since the risk of asphyxia increases with increased duration of second stage of labor (100).

It is important that we have an interpretation template that is safe for use during labor. A high sensitivity reduces the risk of asphyxia, and a high specificity reduces the risk of unnecessary interventions. For classification pathological the SWE09 had the highest sensitivity in both the first and second stage of labor, but it had a low sensitivity in the second stage of labor. The FIGO15 and the SWE17 had too low sensitivities for classification pathological both in the first and second stage of labor to be safe for use, but they had higher specificities. The results were in concordance to previous studies of the FIGO15 and SWE17 (35, 109). If combining pathological and suspicious for sensitivity the SWE17 had a sensitivity close to that of classification pathological with SWE09, but with a higher specificity. When the SWE17 is used in clinical practice it is important to react even at suspicious patterns. The FIGO15 classifies to many tracings as suspicious leading to poor diagnostic precision regardless of if pathological or pathological and suspicious patterns combined are considered as a positive test.

Paper III

Results

CTG tracings were scrutinized for accelerations. The last part of the tracings before birth in acidemic neonates and tracings from the corresponding stage of delivery in non-acidemic neonates were included. The study consisted of 1095 CTG tracings, 364 from cases and 731 from controls. All acidemic neonates born during the study period fulfilling the inclusion criteria of Study III were included. Accelerations were divided in sporadic (no association to contractions) and periodic (coinciding with contractions).

It was more common with sporadic accelerations in controls, both in the first and second stage of labor, Figure 13. With sporadic accelerations present the OR for acidemia was 0.05 in the first stage and 0.09 in the second stage of labor. Presence of periodic accelerations was not as common and had a weaker association to acidemia.

Normal variability was seen in most cases (79%) and controls (98%). An absent variability (0-1 bpm) was strongly associated with acidemia, OR 43.2 (13.4-139). An increased variability lasting for 30 minutes was an uncommon pattern in both cases (1.6%) and controls (0.6%).

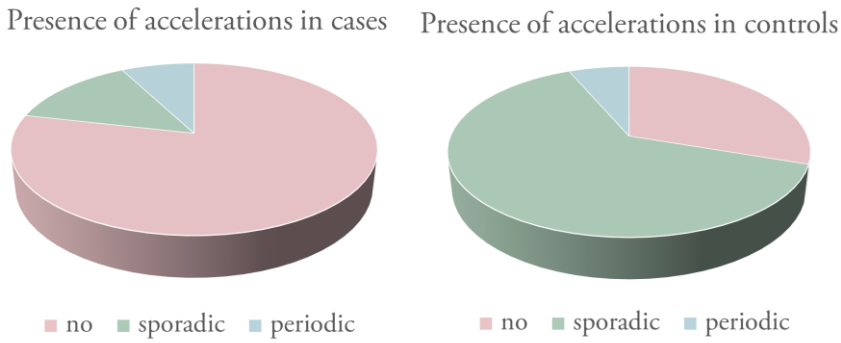


Figure 13. Presence of accelerations in cases and controls
First and second stage combined. Presence of accelerations divided into sporadic accelerations, periodic accelelerations or no present accelerations.

Of the controls 37% lacked sporadic accelerations. Monitoring with scalp electrode and the second stage of labor were associated with the absence of sporadic accelerations. The presence of accelerations according to stage of labor for cases and controls is shown in Figure 14.

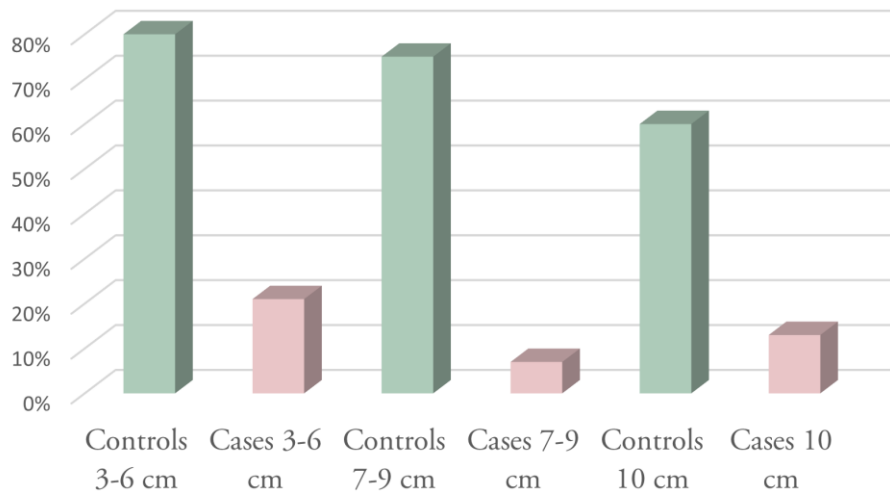


Figure 14. The presence of sporadic accelerations according to cervical dilation.
The presence of sporadic accelerations in % are shown according to cervical dilation for cases and controls.

When combining the presence of sporadic accelerations and variability it was found that the lack of accelerations even with normal variability gave OR 10 for acidemia, however this was a common pattern even in controls (35%).

Since many of the controls lacked sporadic accelerations the PPV for absence of accelerations is low, about 2.2%, but the NPV 99.7%, if the rate of asphyxia is set at 1% of the neonates.

Comments

A CTG tracing with sporadic accelerations present, strongly decreases the risk of acidemia in neonates. This is in concordance to previous studies where it has been found that neonates with accelerations in their CTGs have normal pH, whereas the lack of accelerations is associated to adverse outcome of the neonate (67, 68, 69, 70, 71).

However, the PPV for lack of accelerations is low since many controls lacked accelerations as well and acidosis at birth is rare.

Accelerations were less common in the second stage of labor even in controls. This implies that it is more important to include accelerations in the assessment in the first than in the second stage of labor. In labor wards scalp electrodes are more often used when tracings are classified as pathological or suspicious. Therefore, the lack of accelerations, may cause the use of a scalp electrode instead of the scalp electrode causing a lack of accelerations. There were no association between oxytocin and accelerations after regression analysis suggesting that it is the contractions and labor that affects the fetus and not the oxytocin on its own, as previously shown (145, 171).

The absence of sporadic accelerations is a weak sign of pathology whereas the presence of sporadic accelerations is a strong sign of normality. It is recommended to conclude what type of accelerations that are present in a CTG tracing since not all rises in fetal heart rate is signs of wellbeing of the fetus (78). This recommendation is strengthened by the study since periodic accelerations did not show the same association to normal pH as sporadic accelerations.

Paper IV

Results

In Paper IV the perceived need for intervention by residents after using the SWE09 and the SWE17 was studied. When residents used the SWE09 they wanted to

intervene in 85% of neonates with acidemia and in 30% of non-acidemic neonates. After using the SWE17 they wanted to intervene in fewer acidemic, 76% (p=0.002), and fewer non-acidemic neonates, 22% (p=0.038), Figure 15.

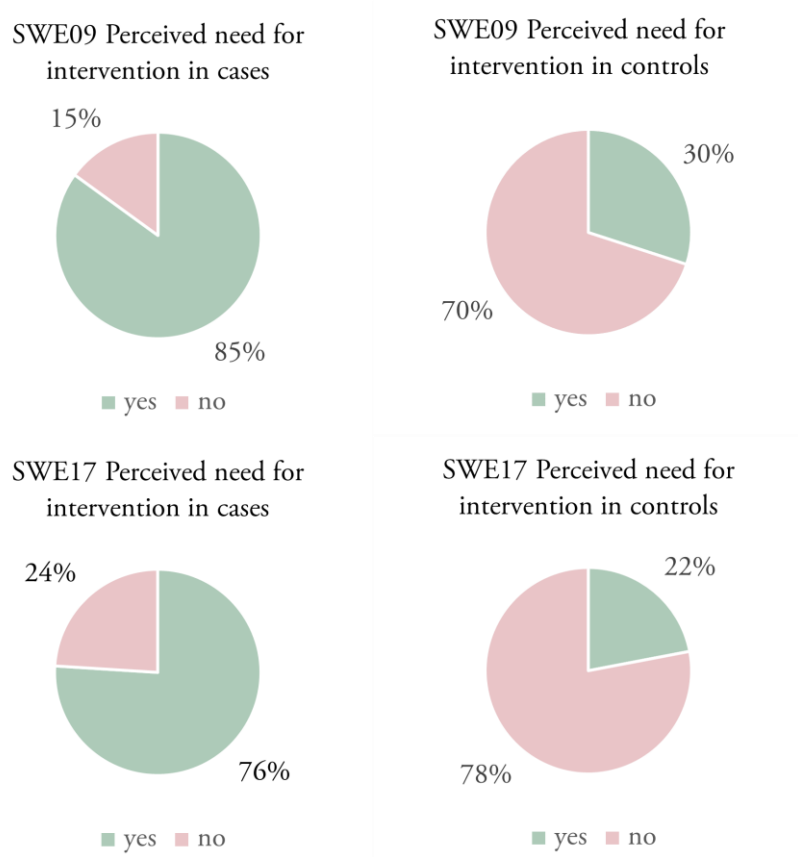


Figure 15. The perceived need for intervention by residents
The perceived need for intervention by residents in cases and controls after using the two templates SWE09 and SWE17.

The sensitivity and specificity for perceived need for intervention after using the two templates were calculated. The SWE09 gave a higher sensitivity (p=0.002) for perceived need for intervention whereas the SWE17 gave a higher specificity (p=0.038).

In Study IV all tracings were assessed by two comparable groups of residents. The sensitivity and specificity were calculated for pathological vs normal and suspicious and for pathological and suspicious vs normal, Table 6.

The SWE09 had a higher sensitivity (p<0.0001), and a lower specificity (p<0.0001), for classification pathological. If classification pathological with SWE09 was compared to classification pathological and suspicious combined with SWE17 the templets sensitivities and specificities did not differ significantly, p=0.44 for sensitivity and, p=0.11 for specificity.

Table 6. Summary of classification according to the two templates SWE09 and SWE17
Calculations are done both for pathological vs normal and suspicious and for pathological and suspicious vs normal.

	Sensitivity Classification pathological % (95% CI)	Specificity Classification pathological % (95% CI)	Sensitivity Classification pathological and suspicious % (95% CI)	Specificity Classification pathological and suspicious % (95% CI)
SWE09[1]	90.6 (86.0-94.1)	53.4 (46.6-60.1)	96.0 (92.5-98.1)	31.8 (25.8-38.4)
SWE17	71.7 (65.4-77.6)	75.8 (69.6-81.3)	88.3 (83.4-92.2)	59.6 (52.3-66.1)

[1] Including patterns classified as preterminal.

When using the SWE17 the residents perceived need for intervention did not differ from the classification pathological with the template (p=0.14, for sensitivity, and p=0.52, for specificity). If pathological and suspicious were combined for sensitivity according to the template the residents perceived need for intervention had a lower sensitivity (<0.0001) and a higher specificity (<0.0001) than the template classification. With the SWE09 the residents perceived need for intervention had a higher specificity (<0.0001) but a lower sensitivity (p=0.002) than the template. The agreement rate between perceived need for intervention and classification was highest for classification pathological with SWE17, κ =0.77.

Comments

When two comparable groups of residents classified CTG tracings their intention to intervene after the classification differed. This implies that the template in use at delivery wards affect clinical decisions. With the SWE09 they didn't want to intervene in 15% of the cases and with SWE17 in 24%. This can partly explain the increase in neonates born with acidemia and low Apgar scores after the implementation of the new template in Sweden (110). The SWE17 also led to a lower rate of perceived need for intervention in controls. This may lead to a lower rate of unnecessary interventions.

An interesting finding was that the residents perceived need for intervention with SWE17 had a higher agreement with classification pathological and that the sensitivity for intention to intervene did not differ from classification pathological

but from classification pathological and suspicious combined. It may be needed to stress the need of observation on suspicious patterns and raise awareness that an FBS or another intervention may be indicated also at suspicious CTG patterns.

Paper I, Paper II, and Paper IV combined

Results and comments

The three studies compared the sensitivity and specificity of CTG interpretation templates, Table 7. The SWE09 had the best combination of sensitivity and specificity in the first stage of labor for classification pathological. In the second stage of labor the SWE17 had the best combination for classification pathological and suspicious combined.

Table 7. Summary of sensitivity and specificity in Paper I, Paper II and Paper IV
Sensitivity and specificty according to the templates. Red numbers are the templates that had the best combination of sensitivity and specificty for the first and the second stage of labor respectively. Blue figures are the sensitivity and specificity closest to current practice.

	Sensitivity Classification pathological % (95% CI)	Specificity Classification pathological % (95% CI)	Sensitivity Classification pathological and suspicious % (95% CI)	Specificity Classification pathological and suspicious % (95% CI)
SWE09[1] First stage	94.5 (86.6-98.5)	90.0 (85.2-93.6)	100 (95.1-100)	75.8 (69.6-81.3)
SWE09[1] Second stage	87.1 (82.8-90.7)	55.5 (51.4-59.6)	97.6 (95.2-99.0)	28.3 (24.7-32.1)
SWE09[1] Residents	90.6 (86.0-94.1)	53.4 (46.6-60.1)	96.0 (92.5-98.1)	31.8 (25.8-38.4)
SWE17 First stage	76.7 (65.4-85.8	96.8 (93.5-98.7)	90.4 (81.2-96.1)	93.2 (89.0-96.1)
SWE17 Second stage	62.0 (56.2-67.6)	84.8 (81.6-87.6)	83.4 (78.6-87.5)	67.7 (63.5-71.4)
SWE17 Residents	71.7 (65.4-77.6)	75.8 (69.6-81.3)	88.3 (83.4-92.2)	59.6 (52.3-66.1)
FIGO15 First stage	71.2 (59.4-81.2)	96.8 (93.5-98.7)	98.6 (91.6-100)	75.3 (69.1-80.9)
FIGO15 Second stage	50.2 (44.3-56.0)	87.5 (84.5-90.0)	96.6 (93.9-98.4)	22.5 (19.2-26.1)

[1] Including patterns classified as preterminal.

The use of SWE17 in Paper IV is the closest to current practice, even if it is a study of only residents in a simulated environment and not true clinical practice. This implies that the use of classification pathological as cut-off is not safe for clinical

practice, due to too low sensitivity. When using suspicious as cut-off for considering an intervention when using the SWE17 it may be safe for safe intrapartum care.

Overall conclusion

In this thesis CTG interpretation templates have been compared. The currently used template in Sweden, SWE17, based on the international FIGO15 template, has a lower sensitivity and a higher specificity than the previously used template SWE09, that was based on the former international template FIGO87. In Paper I and II the FIGO15 was part of the comparison.

I. The second stage of labor. The FIGO15 had a too low sensitivity to be safe to use. The SWE09 had a high sensitivity but a low specificity. The SWE17 had a too low sensitivity for classification pathological but when including suspicious patterns as a pattern that needs attention the sensitivity increased to a useful level without losing too much specificity.

II. The first stage of labor. The findings were similar to those of Paper I. The SWE17 and the FIGO15 had too low sensitivities for classification pathological to be safe to use. In the first stage of labor the SWE09 were concluded to be the safest for use in clinical practice due to a combination of a high sensitivity and a high specificity.

III. The presence of sporadic accelerations indicated a very low risk of acidemia, whereas the lack of accelerations was a weak sign of pathology. Periodic accelerations were a rare pattern, and the presence of periodic accelerations did not lower the risk of acidemia. Sporadic accelerations were less frequent in the second stage of labor even in non-acidemic neonates. An absent variability was highly associated with acidemia.

IV. The perceived need for intervention differed depending on what template that was used. The SWE09 had a higher sensitivity both for perceived need for intervention and for classification pathological and the SWE17 had a higher specificity. The residents considered a need for an intervention when a tracing was classified as pathological with SWE17.

Clinical implications

The three included templates, SWE09, FIGO15, and SWE17, were all introduced without prior evaluation. The SWE17 was implemented in Sweden during 2018 and is now the template in use in Swedish delivery wards.

In this thesis the three templates have been evaluated. The results indicate that the FIGO15 is not safe for intrapartum care due to a too low sensitivity for classification pathological and a too low specificity for classification pathological and suspicious combined. The template leads to a too high proportion of suspicious patterns, both in acidemic and non-acidemic neonates, to be useful in clinical practice.

The SWE09 that was used in Sweden prior to the implementation of the SWE17 had the highest sensitivity for classification pathological. However, the specificity was low in the second stage of labor. If the classification template is used as an alerting system, a pathological pattern must not imply a need of action, but for attention and observation. If an intervention is needed FBS is used in Sweden as a secondary method to CTG that will increase the specificity. In the first stage of labor, where intermittent surveillance with CTG is used it is of high importance not to miss acidosis or even pre-acidosis. Therefore, higher demands for normality are needed. The SWE09 may be the best to use in the first stage of labor of the three guidelines.

The SWE17 that is currently used in Sweden is only safe to use in clinical practice if suspicious patterns are paid attention to. Paper IV indicates that suspicious patterns may not be seen as an indication to intervene. There is a need for alerting suspicious patterns in training and clarifying that a suspicious pattern may indicate acidemia and therefore a potential need for an FBS or delivery.

The assessment of accelerations, assessing type and presence, should be a part of CTG interpretation templates, to improve specificity, by ruling out acidemia. Sporadic accelerations are a positive sign whereas periodic accelerations are an indifferent pattern.

Our findings suggest that CTG may be assessed differently in the first and second stage of labor and that with the SWE17 even a suspicious pattern may need attention.

Future perspectives

CTG is the main method of fetal surveillance during delivery in the developed world. The benefits of CTG have been hard to prove, but today we would not be able to be without it. The CTG tracings are graphs of the fetal heart rate. The tracings must be understood to be useful. The different templates are attempts to put labels on the variation of the fetal heart rate, to make it more understandable.

The existing templates are not perfect. Can we make them better? Analyzing the different variables and then building a template is a step on the way. The next template to be introduced in Sweden must be tested before introduction. To evaluate before a national implementation must be a goal in the future. CTG is not a perfect method to prevent asphyxia. What can we do to improve the method? Since CTG has a low specificity, secondary methods may be needed. The use of FBS will probably continue in Sweden.

AI is upcoming in all fields. How can we use that with CTG? AI is built by humans; can it be better than humans? We can add thousands of patterns and the outcome of the neonate and let the system alert us when patterns that are associated to acidemia occurs. Will this be part of our daily use of CTG in the future? An AI system can also read the medical file and help us find the neonates and mothers at risk. A system that alerts us when the fetus isn't growing or the blood pressure of the mother increases. This kind of system is used in some primary care units today, will it be a part of our care tomorrow?

Not all fetuses and mothers are the same. A differentiated delivery care may be needed. Our care is optional. A family that wants to say no to CTG or other parts of our care are entitled to do so, but it should be after information, and it should be because the family wants it. Will we have more options to our delivery care in the future? Maybe, if there are enough mothers who want it.

I believe that CTG will continue to be our main method of fetal surveillance since we don't have any alternative methods shown to be superior. I believe that CTG will be used with the help of other methods such as FBS. I also believe that we will have an alert system that is useful with the help of AI, both in pattern recognition and in finding deliveries at risk. I believe that we must continue trying to recognize the fetal heart rate of a fetus at risk for acidemia and that we need to develop a new template with high sensitivity and high specificity for safe intrapartum care, and that all new templates and methods must be evaluated before wide implementation.

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