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Computerized analysis of cardiotocograms in clinical practice and the SisPorto® system thirty-two years after: technological, physiopathological and clinical studies

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Abstract

Objectives: The objective of this study is to present the why, what and how about computerized analysis of cardiotocograms (cCTG) and the SisPorto system for cCTG.

Content: A narrative review about cCTG and the SisPorto system for cCTG is presented. The meta-analysis of randomized controlled trials (RCT) performed so far have evidenced that cCGT compared to traditional CTG analysis may save time spent in hospital for women, in the antepartum period, and is objective with at least equivalent results in maternal and perinatal outcomes, both in the ante and intrapartum periods. The SisPorto system for cCTG closely follows the FIGO guidelines for fetal monitoring. It may be used both in the ante and intrapartum periods, alone or connected to a central monitoring station, with simultaneous monitoring of fetal and maternal signals, not only in singletons but also in twins. It has been assessed in technical, physiopathological and clinical studies, namely in one large multicentric international RCT during labor and two meta-analysis.

Summary and outlook: There is evidence that cCTG may be useful in clinical practice with advantages compared to traditional CTG analysis, although without clear impact on the decrease of preventable maternal and perinatal mortality and morbidity. More studies are warranted, namely on technical improvements and assessment in larger studies in a wider range of clinical settings.

Keywords: cardiotocograms; cardiotocography; computerized analysis; fetal heart rate; fetal monitoring; omniview-sisporto; Oxford system; SisPorto; Sonicaid system.

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Introduction

The first paper, or, at least, one of the first papers, published in an indexed peer reviewed journal, that has described a commercially available system for computerized analysis of cardiotocograms (cCTG) was issued in 1991 [1]. The paper addressed the typical why, what and how questions that led to the development of the Sonicaid system 8,000® by Dawes and Redman after more than ten years of research [1]. The system, that was initially commercialized by the Oxford Sonicaid Ltd., UK, and is now commercialized by the Huntleigh Healthcare company, UK, has been widely disseminated in clinical practice in the antepartum period. It has been assessed in several studies, including two randomized controlled trials (RCT) [2, 3] and two meta-analysis [4, 5]. It is objective and may reduce the time spent in hospital and further investigations for women, in high-risk pregnancies, despite no clear evidence that it could reduce preventable perinatal mortality and morbidity [4, 5].

In the same year 1991, a paper with the first cases analysed by the Porto System for cCTG [6], later commercialized as the SisPorto® [7] and the Omniview-SisPorto® (Speculum, Portugal) [8], was also published in an indexed peer reviewed journal [6]. The system has been so far mainly disseminated in clinical practice in the intrapartum period, but it has also been used in the antepartum [7, 8].

In this paper, answers to the why, what and how questions that have justified the continued development of cCGT in clinical practice and of the SisPorto® system are presented.

Methods

A narrative review about the why, what and how about cCTG in clinical practice and the SisPorto® system for cCTG is presented. Tables were developed to summarize the results of the main systematic reviews about the present state of the CTG analysis and the cCTG in clinical practice (Table 1), as well as the main results obtained so far with the SisPorto® system (Tables 2–4). Additionally, a figure is presented to display some of the peculiarities of the systems for cCTG used in clinical practice (Figure 1).

Results

Why cCTG in clinical practice?

An initial will for improvement

The idea of the use of computers in CTG analysis was almost contemporary to the initial development and dissemination of cardiotocography in clinical practice, in the decades of 1970 and 1980, as a will for improvement of the technique [9, 10]. However, CTG analysis was disseminated in clinical practice, with a wide acceptance of conventional visual analysis of tracings, without a significant development of cCTG [11]. At that time, the cost, scarcity, dimensions, processing speed and programming complexity of the computers were major obstacles to the development of cCTG [12]. In that way, visual estimation of the FHR baseline, decelerations, accelerations, short and long-term variability, without cCTG, became the standard way of assessing CTGs, both in the ante and intrapartum periods [11].

A compelling challenge

In the final years of the decade of 1980, cCTG became a compelling challenge to overcome the evidence that visual analysis of CTGs was poorly reproducible [13–15], with discrepant results of sensitivity and specificity, in the detection and prevention of the same or different outcomes [16, 17]. Not surprisingly, the results of the meta-analysis studies, combining results from randomized controlled trials (RCT) that had used methods with discrepant sensitivities and sensitivities, did not evidence clear differences between visual analysis of CTGs and other methods, such as intermittent auscultation (Table 1) [5, 18–20]. In this setting, a meta-analysis by Grivel et al. [5] showed that in the antepartum period visual CTG analysis vs. no CTG analysis showed no significant difference in perinatal mortality (2.3% vs. 1.1%, 4 studies, n=1,627) or preventable deaths, though the meta-analysis was underpowered. In the same line, there was no significant difference in caesarean sections (19.7% vs. 18.5%, 3 trials, n=1,279). There was also no significant difference for 5 min-Apgar scores <7 or admission to neonatal intensive care units [5]. Similarly, the meta-analysis published by Neilson et al. [19] and Alfirevic et al. [20], regarding studies performed in the intrapartum period, showed that visual CTG analysis during labor was associated with reduced rates of neonatal seizures, but no clear differences in cerebral palsy, infant mortality or other outcomes. Moreover, continuous CTG analysis was associated with an increase in caesarean sections and instrumental vaginal births, even when there was access to fetal blood sampling [20]. On the other hand, ST waveform analysis made no obvious difference to caesarean sections (6 trials, n=26,446), severe metabolic acidosis or neonatal encephalopathy [19]. There were, however, fewer fetal scalp samples, although the findings were heterogeneous. Moreover, there were marginally fewer operative vaginal births but no obvious difference in low 5 min-Apgar scores or admissions to special care units [19]. There was little evidence that PR interval analysis conveyed any benefit [19].

What system for cCTG in clinical practice?

A system for cCTG for clinical practice has to be affordable, reliable, user-friendly, understandable by the health professionals and capable of improving maternal and perinatal outcomes. This has only become possible after the introduction of modern personal computers [1, 21].

How to develop and validate a cCTG system for clinical practice?

Physiological and physiopathological background–the importance of the FHR baseline

Medical decisions are based on the knowledge of physiopathology and in probabilities. Accordingly, it is reasonable to develop systems for cCTG based not only on the analysis of mathematical variables used in the calculation of probabilities but also on physiopathological models translated from experimental studies understandable by clinicians [22].

Thus, it is important that cCTG systems are developed as to allow clinicians to analyse what they are familiar

Table 1: Summary of the systematic reviews of clinical studies on the use of traditional cardiotocography (CTG) and computerized CTG (cCTG), in the antepartum and intrapartum settings.

Setting	Authors	Title of the systematic review	Studies and cases included in the systematic review	Main objectives, results and conclusions
Antepartum	Grivell et al. [4]	Antenatal CTG for fetal assessment. Cochrane Database Syst Rev	6 RCTs or quasi-RCTs involving 2,105 high-risk pregnancies	Traditional CTG vs. no CTG showed no significant difference in perinatal mortality (2.3% vs. 1.1%, 4 studies, n=1,627) or preventable deaths, though the meta-analysis was underpowered. Similarly, there was no significant difference in caesarean sections (19.7% vs. 18.5%, 3 trials, n=1,279) nor in 5 min-apgar scores <7 or admission to neonatal intensive care units There were no eligible studies that compared cCTG with no CTG Compared to traditional CTG, cCTG showed a significant reduction in perinatal mortality (0.9% vs. 4.2%, 2 studies, n=469). However, there was no significant difference in preventable deaths (2 studies, n=469), though the meta-analysis was underpowered. There was no significant difference in caesarean sections (63% vs. 72%, 1 study, n=59) nor in 5 min-apgar scores <7 (2 studies, n=469)
Antepartum	Baker et al. [5]	Comparison of visual and antenatal cCTG in the prevention of perinatal morbidity and mortality. A systematic review and meta-analysis	3 RCTs (n=497) and 3 non-RCT (n=1,265)	In high-risk pregnancies, cCTG was associated to a non-significant reduction in all-cause perinatal mortality and cesarean sections, in the RCTs. However, there was only one antenatal stillbirth across the RCTs. In the non-RCT the analysis was not possible. Despite no clear reduction in perinatal mortality and morbidity, cCTG is objective and may reduce time spent in hospital and further investigations for women
Intrapartum	Neilson [19]	Fetal electrocardiogram (ECG) for fetal monitoring during labour. Cochrane Database Syst Rv	7 RCTs involving 27,403 women: 6 trials of ST analysis (n=26,446) and 1 trial of PR interval (n=957)	ST analysis made no obvious difference to caesarean sections (6 trials, n=26,446), severe metabolic acidosis or neonatal encephalopathy. There were, however, fewer fetal scalp samples although the findings were heterogeneous. There were marginally fewer operative vaginal births but no obvious difference in low 5 min-apgar scores or admissions to the special care units. There was little evidence that PR interval analysis conveyed any benefit
Intrapartum	Alfirevic et al. [20]	Continuous CTG as a form of electronic fetal monitoring for fetal assessment during labour. Cochrane Database Syst Rev	13 RCTs or quasi-RCTs involving over 37,000 women: 12 trials compared intermittent auscultation with continuous CTG; 1 trial	Traditional CTG during labour is associated with reduced rates of neonatal seizures, but no clear differences in cerebral palsy, infant

Table 1: (continued)

Setting	Authors	Title of the systematic review	Studies and cases included in the systematic review	Main objectives, results and conclusions
			compared intermittent with continuous CTG	mortality or other outcomes. However, continuous CTG was associated with an increase in caesarean sections and instrumental vaginal births. Access to fetal blood sampling did not appear to influence the results
Intrapartum	Balayla et al. [55]	Use of artificial intelligence in the interpretation of intrapartum FHRtracings: a Systematic review and meta-analysis	3 RCTs (n=55,064) compared the maternal and neonatal outcomes with cCTG or traditional CTG. 6 cohort studies assessed the agreement between experts and cCTG	cCTG did not change the rates of neonatal acidosis, UAB pH<7.20, 5 min APGAR scores <7, mode of delivery, NICU admission, neonatal seizures, or perinatal deaths (3 studies, n=55,064). On the other hand, a weighed mean Cohen's kappa of 0.49 (0.32–0.66) was obtained in the assessment of agreement between experts and computerized systems (6 studies)
Intrapartum	Campanile et al. [56]	Intrapartum CTG with and without computer analysis: a Systematic review and meta-analysis of RCTs	3 RCTs (n=54,492) compared the maternal and perinatal outcomes in women monitored with cCTG or traditional CTG	All the RCTs enrolled women with cephalic presentation at term or late preterm. Women who received continuous cCTGduring labor had similar risk of newborn metabolic acidosis. No between group differences were found in the secondary outcomes

RCT, randomized controlled trials; FHR, fetal heart rate; UAB, umbilical artery blood.

with. Namely the dynamics of the sympathetic and parasympathetic system in response to hypoxic, haemodynamic or other stimuli, by the identification of the FHR baseline, accelerations, decelerations and short and long-term variability [11, 22]. That will enable clinicians to anticipate and establish diagnosis, prognosis and therapeutic actions, not only based on the analysis of probabilities, performed either by humans or computers, but also based on the knowledge of what happens in the physiopathological processes.

In this setting, the definition of a measurable FHR baseline with a physiopathological meaning is crucial. Not only because of the intrinsic physiological and physiopathological meaning of the baseline but also because it is a prerequisite for the estimation of all the other CTG variables, namely the accelerations and decelarations [11, 22]. In this way, the definition of an objective FHR baseline, early became the main challenge of the development of the Porto system/SisPorto® for cCTG [6, 23–25]. A FHR baseline with a physiological and physiopathological meaning was developed, rather than an abstract mathematical concept or an equivocal concept interdependent of the definition of the accelerations and decelerations [26, 27]. A FHR baseline indexed to the basal FHR obtainable during fetal rest, that is, during calm fetal sleep (fetal behavioral state 1F) in the absence of fetal movements, uterine contractions, drug actions or other abnormal stimuli [26, 27]. A FHR baseline indexed to the mean FHR value of a FHR pattern A, corresponding to the cardiac intrinsic cronotropic activity under the influence of a resting autonomous and central nervous system [27]. That FHR baseline is not only meaningful from the physiological and physiopathological point of view, but is also measurable in the most reproducible way ever reported in CTG analysis [27]. Then, from that FHR baseline, accelerations, decelerations and variability may be objectively estimated [23, 24, 28, 29]: accelerations corresponding to the activation of the central nervous system (fetal behavioral states) or to the response of the sympathetic branch of the autonomous nervous system to the stimulation of the baro or chemo receptors; decelerations corresponding to the activation of the parasympathetic branch of the autonomic nervous system via the baro or chemo receptors or to a depression or blockade of the intrinsic cardiac activity; and variability corresponding to the permanent balance action of the central and the autonomic nervous system over the

Table 2: Summary of representative studies performed with the SisPorto® system in relation to technological developments.

Authors	Populations	Study design	Main objectives, results and conclusions
Bernardes et al. [6]	70 cases	Case series	First description of the porto system hardware, signals acquisition, pre-processing and processing algorithms according to the FIGO guidelines
Bernardes et al. [23]	NA	Descriptive	Updated version of the FHR baseline algorithm of the porto system with analysis of typical FHR patterns (A, B, C, D, accelerative-decelerative, decelerative, largely decelerative and flat/sinusoidal)
Marques de sá et al. [24]	145 CTGs: 85 for training and 60 for testing	Case series	The estimation of FHR baselines using artificial neural networks was correct in 97.6% in the training set and in 83.3% in the testing set
Felgueiras et al. [44]	124 FHR sequences: 31 patterns A, 50 B and 43 FS (Flat/Sinusoidal)	Case series	Using temporal fractal features of FHR sequences, a good classification performance of the FHR patterns A, B and FS was obtained with errors between 7 and 16%
Ayres-Campos et al. [7]	NA	Narrative review	Description of an updated version of the system (SisPorto® 2.0) with a summary of the results of the clinical studies
Gonçalves et al. [39]	33 CTGs from 33 fetuses simultaneously acquired with internal ECG and external US in the intrapartum period	Case series	The mode used to acquire FHR signals (ECG or US) and the sampling rate employed (2 or 4 Hz) can significantly affect most FHR indices. The correlation between the FHR sampled at 2 or 4 Hz was high for both linear and nonlinear indices but nonlinear index values were significantly higher at 2 Hz
Ayres-Campos et al. [8]	NA	Descriptive	Description of an updated version of the system including a central fetal monitoring station (Ominiview-SisPorto®)
Amorim-Costa et al. [34]	All CTGs recorded in randomly selected days of years 2006 and 2009, in the ante and intrapartum periods	Case series	Antepartum CTGs had a correct patient identification in 92% of the cases, while the mean signal loss fell from 7.4% in year 2006 to 5.8% in 2009 ($p=0.012$). Intrapartum CTGs had a correct identification in 44% of cases in year 2006 and in 69% in 2009 ($p<0.001$), while the mean interval between tracing-end and birth decreased from 12.0 in year 2006 to 8.4 min in year 2009 ($p<0.001$). All the retrieved CTGs matched the original paper recordings
Gonçalves et al. [38]	27 CTGs from 27 fetuses with simultaneous beat-to-beat and 4 Hz sampling rate (21 fetuses with UAB pH≥7.20 and 6 with UAB pH<7.20	Case series	Using a scalp electrode, beat-to-beat sampling provided significantly better results in linear indices and 4 Hz sampling in entropy indices, regarding the discrimination between fetuses born with different UAB pHs
Nunes et al. [36]	33 CTGs from 33 fetuses with simultaneous external and internal monitoring during the second stage of labor	Case series	A higher signal loss was observed with external monitoring (10% vs. 4%; $P<0.001$). No differences were found in mean FHR baseline (129 bpm vs. 130 bpm, $P=0.245$), but more accelerations (12 vs. 8, $P<0.001$) and less decelerations (8 vs. 10, $P<0.001$) were detected with external monitoring
Pinto et al. [35]	40 1 h CTGs from 20 women during the last 2 h of labor	Case series	Description of algorithms for computer analysis of MHR during labor. There was a statistically significant inter-observer and computer-observer agreement and reliability in estimation of basal MHR, accelerations, decelerations and LTV, with PA values ranging from 0.72 (95% CI: 0.62–0.79) to 1.00 (95% CI: 0.99–1.00), and K values ranging

Table 2: (continued)

Authors	Populations	Study design	Main objectives, results and conclusions
			from 0.44 (95% CI: 0.28–0.60) to 0.89 (95% CI: 0.82–0.96)
Pinto et al. [41]	61 MHR and FHR recordings simultaneously acquired in the final hours of labor	Case series	Seventy-two percent of tracings exhibited episodes of major MHR-FHR ambiguities, which were associated with MHR accelerations, FHR signal loss and decelerations. Removal of MHR-FHR ambiguities resulted in a significant decrease in FHR decelerations, and improvement in FHR tracing classification, regarding the prediction of the UAB pH
Gonçalves et al. [37]	51 MHR recordings from 51 women simultaneously acquired with ECG and photoplethysmography (PPG)/oximetry during the last 2 h of labor	Case series	MHR variability indices were significantly different with ECG and PPG, with high disagreement for entropy and fast oscillation indices, and low disagreement for the mean MHR and slow oscillation indices. However, both acquisition modes evidenced comparable auROC values in the detection of fetal acidemia and operative vaginal delivery
Ayres-Campos et al. [33]	NA	Descriptive	Description of the SisPorto® 4.0 – computer analysis following the 2015 FIGO guidelines for intrapartum fetal monitoring

NA, not applicable; CTGs, cardiotocograms; FHR, fetal heart rate; ECG, electrocardiography; MHR, maternal heart rate; LTV, long term variability; FIGO, international federation of gynecologists and obstetricians; auROC, area under receiver-operator curve; ECG, electrocardiography; US, ultrasonography; PA, proportions of agreement; 95% CI, 95% confidence interval.

cardiac activity [30–32]. Figure 1 displays a cCTG performed by the Omniview-SisPorto®, with simultaneous recording of the maternal heart rate (MHR) and FHR. At the bottom of Figure 1, the results of the "Last hour analysis" are presented, with indication of: the signal loss and quality; the basal MHR and FHR (right columns of the results) and the MHR and FHR baselines (indexed to the basal MHR and FHR–left columns of the results); the accelerations, the decelerations and the abnormal short (STV) and long term variability (LTV); and the uterine contractions (UC).

Equipment, signals acquisition, storing and retrieving

The development and dissemination of conventional fetal monitors with facilities for the communication with user-friendly low-cost personal computers were, and are, essential for the development of cCTG [1, 6, 21]. Initially the communication between fetal monitors and personal computers was established via digital ports and cables [1, 6, 21]. Now everything is more flexible with local and remote wireless intra and internet facilities.

Modern conventional fetal monitors convey maternal and fetal signals in a digital format. MHR may be acquired via electrocardiographic (ECG) or photoplethysmography (PPG)/oximetry sensors, while maternal temperature and blood pressure may be also acquired (Figure 1). On the other hand, FHR may be acquired with external or internal ECG sensors or external ultrasound probes (US). UC may also be acquired with internal sensors or external tocodynamometry [6–8, 33–35].

In Table 2, the most representative studies performed with the SisPorto® system in relation to technological developments are summarized.

It is important to consider the kind of sensors that are used to get the maternal and fetal signals. Nunes et al. observed a higher signal loss with external monitoring with US compared to internal ECG sensors (10% vs. 4%; $p<0.001$) [36]. However, no differences were found in mean FHR baseline (129 bpm vs. 130 bpm, $p=0.245$), though more accelerations (12 vs. 8, $p<0.001$) and less decelerations (8 vs. 10, $p<0.001$) were detected with external monitoring [36]. One the other hand, Gonçalves et al. found that MHR variability indices were significantly different when obtained with ECG or PPG/oximetry sensors, with high disagreement, for entropy and fast oscillation indices, and low disagreement, for the mean MHR and slow oscillation indices [37]. However, both the acquisition modes evidenced comparable auROC values in the prediction of neonatal acidemia and operative vaginal delivery [37] (Table 2).

Table 3: Summary of representative studies performed with the SisPorto® system in relation with physiological and physiopathological variables and processes.

Authors	Populations	Setting	Type of study	Study design	Main objectives, results and conclusions
Bernardes et al. [24]	NA	Ante and intrapartum	Review	Narrative	Updated version of the system with a summary of the physiological and physiopathological background of their algorithms
Pereira-Leite et al. [55]	110 CTGs from 17 twin pregnancies	Antepartum	Descriptive	Case series	The median signal loss was 8% (95% CI: 4–13). The median differences between FHR baselines, accerelarions, decelerations and abnormal LTV were: 4bpm (95% CI: 1–6%), 4 (95% CI: 1–7), 0 (95% CI: 0–1) and 0 (95% CI: 0–2). The high similarity between twin tracings show how easily they can be confused
Ayres-Campos et al. [27]	150 ante and 150 intrapartum unselected CTGs from the same number of fetuses, analysed by 3 experienced clinicians	Ante and intrapartum	Agreement and reliability	Case series	The agreement and reliability of the FHR baseline estimated by SisPorto®® 2.01 was excellent compared to a consensus of clinicians, with proportions of agreement and K statistic of 0.97 and 0.97 in the antepartum and 0.89 and 0.87 in the intrapartum, respectively
Gonçalves et al. [45]	50 antepartum CTGs from 50 fetuses with normal outcomes	Antepartum	Descriptive	Case series	FHR patterns associated to active sleep (pattern B) and wakefulness (pattern D) evidenced more signs of autonomous nervous system activity, with sympatho-vagal imbalance, and less signs of complexity than patterns associated with calm sleep (pattern A) and wakefulness (pattern C)
Bernardes et al. [48]	36 and 30 CTGs from the same number of female and male non-acidemic and acidemic fetuses	Intrapartum	Descriptive	Case series	Term female fetuses exhibited significantly more linear FHR activity than their male counterparts, while maintaining similar complex activity, in the final minutes of labor and when born with acidosis
Costa et al. [29]	206 h of CTGs from 50 consecutive cases	Intrapartum	Agreement and reliability	Case series	The agreement between the computer and a consensus of clinicians was high in FHR baseline estimation (ICC=0.85, with a mean difference of 3.7 bpm). Moreover, a concordant identification was observed in 71% of accelerations, 68% of decelerations and 87% of uterine contractions
Amorim-Costa et al. [49]	9,701 CTGs from fetuses from 24 to 41 weeks	Antepartum	Descriptive	Case series	Gender-specific reference charts for CTG parameters throughout normal pregnancy, from 24 to 41 weeks evidence a decrease of FHR baseline and an increase of accelerations and variability; decelerations were practically zero for all gestational ages. The FHR baseline was consistently higher in females whereas variability was lower
Gonçalves et al. [46]	4,713 male and 4,110 female fetuses, with normal pregnancy outcomes, with gestational ages from 25 to 40 weeks	Antepartum	Descriptive	Case series	Mean FHR decreased significantly throughout gestation, whereas most variability indices increased. Sympatho-vagal imbalance exhibited two local maxima at 29–30 and 34–35 weeks and decreased afterwards. Entropy indices increased until around the 34th week, slightly decreasing after the 37th week. Female fetuses

Table 3: (continued)

Authors	Populations	Setting	Type of study	Study design	Main objectives, results and conclusions
					presented higher mean FHR and entropy from the 34th week afterwards, and lower short-term variability and sympatho-vagal balance in the same period
Amorim-Costa et al. [50]	1,049 CTGs longitudinally acquired in 145 female and male fetuses	Antepartum	Descriptive	Cohort	During pregnancy, FHR baseline and number of decelerations decreased. Conversely, FHR variability, accelerations and uterine contractions increased. There was a high inter-fetal variability, but there was intra-fetal consistency. Fetuses showing a marked decrease in FHR baseline and those with a marked increase in average LTV had a significantly lower birthweight
Amorim-Costa et al. [51]	1,276 CTGs from 176 fetuses of which 207 from 31 small for gestational age (SGA) fetuses	Antepartum	Descriptive	Cohort	During pregnancy, FHR baseline showed a more pronounced decrease in SGA fetuses, being higher at earlier gestational ages and lower later. Average LTV was significantly lower in SGA<p3 fetuses, but a parallel increase occurred in all groups. There was considerable inter-fetal variability within each group
Tendais et al. [54]	14 twin pairs	Antepartum	Descriptive	Case series	Male-male twins had signs compatible with the most active autonomic nervous system and male-female twins with the most active complexity system

NA, not applicable; CTGs, cardiotocograms; FHR, fetal heart rate; LTV, long term variability; 95% CI, 95% confidence intervals; ICC, intraclass correlation coefficient.

It is also important to consider how maternal and fetal signals are sampled by the computer from the fetal monitor digital ports. According to Gonçalves et al., using a scalp electrode, beat-to-beat sampling provided significantly better results in the estimation of FHR linear indices and 4 Hz sampling better results in entropy indices, regarding the discrimination between fetuses born with different umbilical artery blood (UAB) pHs [38].

Preprocessing algorithms

After the maternal and fetal signals acquisition by the computer, it is important to pay attention to the preprocessing algorithms. They correct errors, remove noise and, if possible, reduce the number of signals to be processed, as to make their storing, processing and display more efficient. The preprocessing algorithms are also important to provide information about signals loss and quality [6–8, 24, 33–35]. However, as the preprocessing algorithms may significantly change the original signals, it is essential to know their possible effect on the final signals processing results.

There are several studies about these less published issues, like a paper by Gonçalves et al. who verified that the resampling at 2 Hz of FHR signals acquired at 4 Hz can significantly affect most FHR variability indices [39].

Another important preprocessing issue pertains to the identification and correction of MHR sequences misrecorded and misinterpreted as FHR sequences, as to avoid severe clinical errors, including fetal deaths [40]. In this setting, Pinto et al. verified that during the final hours of labor of 61 laboring women, 72% of the FHR tracings exhibited episodes of major MHR-FHR ambiguities. The removal of MHR-FHR ambiguities resulted in a significant decrease in the detection of FHR decelerations and an improvement in FHR tracing classification, regarding the prediction of the newborn UAB pH [41] (Table 2).

Processing algorithms following the FIGO guidelines for fetal monitoring

The use of processing algorithms for CTG analysis closely following international guidelines is important to make the systems for cCTG understandable by the health

Table 4: Summary of representative studies performed with the SisPorto® system in relation with clinical studies of diagnosis, prognosis and effectiveness.

Authors	Populations	Setting	Type of study	Study design	Main objectives, results and conclusions
Montenegro et al. [57]	7 fetuses with severe FGR	Antepartum	Validity	Cohort	Non-invasive assessment of the hypoxic fetus with color Doppler and cCTG allowed the documentation of the progressive deterioration of the fetal condition and of the possibility of intervention
Bernardes et al. [58]	42 ante and 43 intrapartum cases	Ante and intrapartum	Validity	Case series	The sensitivities and specificities of a semi-automated version of the SisPorto®® system ranged between 79% (95% CI: 60–92%) and 100% (95% CI: 95–100%), in relation to several compound outcomes, combining 1 and 5 min apgar scores and UAB pH
Ayres-Campos et al. [59]	345 cases from 8 tertiary care centres in Europe and Australia, 4 h before an elective cesarean section	Antepartum	Validity	Multicentre case series	The auROC regarding the prediction by SisPorto®® of the 1 and 5 min apgar scores under 5 and 7 respectively, were 0.96–1.00 and 0.81–0.89. The best auROC regarding the prediction of an UAB pH<7.15 was 0.69
Gonçalves et al. [61]	48 non-acidemic, 10 mildly acidemic and 10 moderatly-severely acidemic fetuses	Intrapartum	Validity	Case series	The best results with linear and nonlinear FHR analysis of normal and acidemic fetuses in the minutes preceding delivery were a specificity of 71% and a specificity of 80%
Costa et al. [62]	148 CTGs with ST analysis from 148 fetuses in the minutes preceeding a vaginal or cesarean	Intrapartum	Validity	Case series	cCTG and ST events provided a sensitivity of 1.00 (95% CI: 0.56–1.00) and a specificity of 0.94 (95% CI: 0.89–0.97), in the prediction of neonatal pH≤7.05.
Costa et al. [63]	204 cases, randomized to computer or non-computer analysis	Intrapartum	Validity	Case series	The access to cCTG in the intrapartum period improved the clinicians' prediction of the newborn UAB pH
Gonçalves et al. [60]	15 severe FGR cases and 18 controls	Antepartum	Validity	Case control	Severe FGR fetuses present gender-specific FHR changes, compared with controls, characterized by a significantly lower entropy and sympathetic-vagal balance in females than in males. High sensitivities and specificities were achieved in the detection of male FGR fetuses at gestational ages less than 34 weeks
Pinto et al. [52]	58 cases with simultaneous recording of MHR and FHR in normal and acidemic fetuses	Intrapartum	Validity	Case series	Combined conventional MHR-FHR analysis may help to improve the prediction of newborn acidemia compared with FHR analysis alone. The auROC ranged between 0.50 for FHR accelerations and 0.77 for MHR baseline plus FHR STV
Gonçalves et al. [52]	51 non-acidemic and acidemic cases	Intrapartum	Validity	Case series	Combined linear and non-linear MHR-FHR analysis may improve the identification of fetal acidemia compared with FHR alone. The inclusion of MHR on bivariate analysis achieved sensitivity and specificity values of nearly 100 and 89.1%, respectively
Gonçalves et al. [64]	32 and 23 CTGs from the same number of normal and operative vaginal deliveries (OVD)	Intrapartum	Validity	Case series	The analysis of UC signals obtained with tocodynamometry, using linear and nonlinear indices, identified significant changes during labor and differences

Table 4: (continued)

Authors	Populations	Setting	Type of study	Study design	Main objectives, results and conclusions
					between normal and OVDs, but the discriminative capacity between the two types of delivery was modest
Nunes et al. [65]	7,730 cases randomized: 3,961 to cCTG and 3,769 to visual analysis	Intrapartum	Effectiveness	RCT	Computer analysis with real-time alerts did not significantly reduce the rate of metabolic acidosis or obstetric intervention. A lower-than-expected rate of newborn metabolic acidosis was observed in both arms of the trial
Lopes-Pereira et al. [66]	38,466 cases: 8,791 before the introduction of Ominiview-SisPorto® and 29,675 after	Intrapartum	Observational	Cohort	Introduction of cCTG and ST signals in a tertiary care hospital was associated with significant reductions in hypoxic-ischemic encephalopathy and cesarean deliveries

FGR, fetal growth restriction; CTGs, cardiotocograms; ST, ST segment of the ECG; FHR, fetal heart rate; MHR, maternal heart rate; STV, short-term variability. FIGO, international federation of gynecologists and obstetricians; auROC, area under receiver-operator curve; 95% CI, 95% confidence interval; UAB, umbilical artery blood.

professionals that are familiar with conventional CTG analysis. This has been the way followed since the beginning of the development of the SisPorto® system that closely follows the FIGO guidelines for fetal monitoring [6–8, 11, 22, 33–35]. In this setting, the most difficult part of the development of the SisPorto® algorithms pertained to the algorithm for the FHR baseline estimation. The FHR baseline is easy to estimate in stable FHR patterns but very difficult to ascertain in unstable FHR patterns, like largely decelerative or accelerative patterns, namely during the fetal behavioral state F4 with FHR pattern D or during second stage of labor [23, 24]. In this way, a complex algorithm, that is described in detail elsewhere [6–8, 23, 24] was developed. Then, algorithms for the detection and classification of FHR accelerations, deceleration and uterine contractions, were developed, as well as for the estimation of FHR short-term (STV) and long-term variability (LTV) [6–8, 23, 24, 33–35] (Table 2 and Figure 1).

Processing algorithms with non-conventional analysis

Modern personal computers allow the calculation of an almost endless number of mathematical non-linear and linear time and frequency domain CTG indices, and their combined use in the prediction of clinical outcomes using multivariate analysis and artificial intelligence tools [42, 43]. Some of those mathematical and computational tools have also been used with SisPorto®, namely linear time and frequency domain indices, and non-linear entropy and fractal indices, as well as combined MHR-FHR analysis and FHR analysis using neural networks [25, 44–48] (Table 2).

Interface with the users, signals display and printing

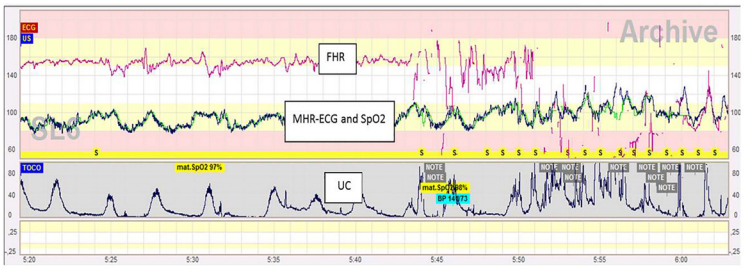
The interfaces of the systems for cCTG have been assumed by their developers as essential for their acceptance and efficacy [1, 6–8]. The SisPorto® system automatically starts signals acquisition and display, as soon as any fetal monitor connected to the system is turned on (Figure 1). The latest Omniview-SisPorto® version provide the online display of up to 16 CTGs in a central monitoring system station emulating conventional colored CTG paper, with its characteristic scales and speeds. Alarms may be set-up at the best convenience and tracings may be printed in the conventional cardiotocographic format [8, 33].

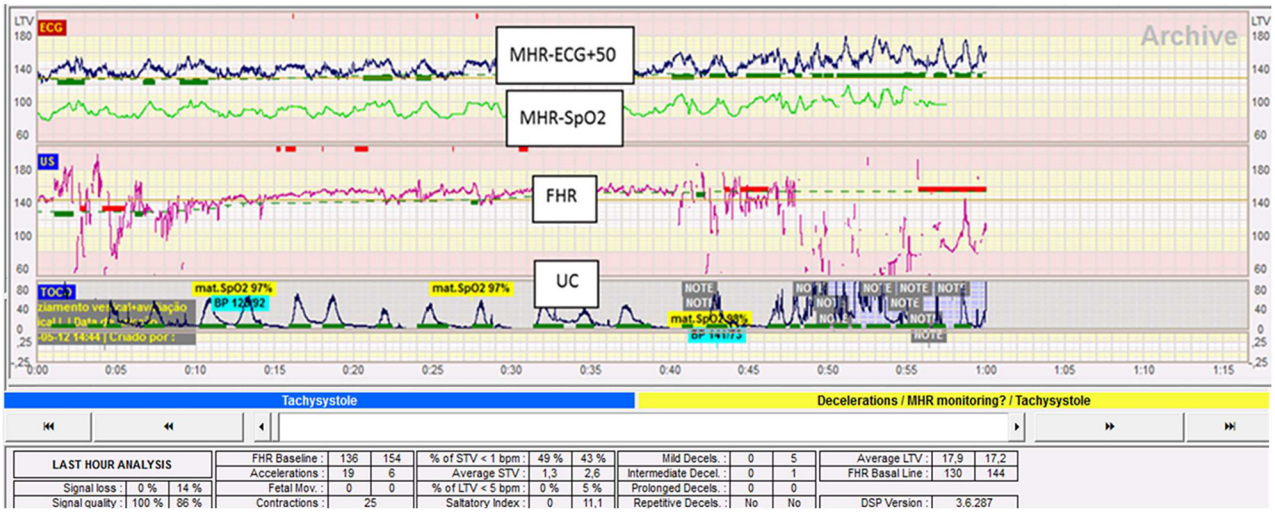
Applications in physiological and pathophysiological studies – fetal behavioral states, fetal development and gender, twin-to-twin and maternal-fetal interactions

Besides the identification of the basic CTG features (Figure 1), the systems for cCTG should be able to identify and characterize other physiological or physiopathological variables and processes.

In Table 3, a summary of the most representative studies performed with the SisPorto® system are presented, in relation to the fetal behavioral states, fetal development and gender, as well as twin-to-twin and maternal-fetal interactions [45–54].

Gonçalves et al. showed that the FHR patterns associated to active sleep (pattern B) and wakefulness (pattern D) evidenced more signs of autonomous nervous system activity, with sympatho-vagal imbalance, and less signs of





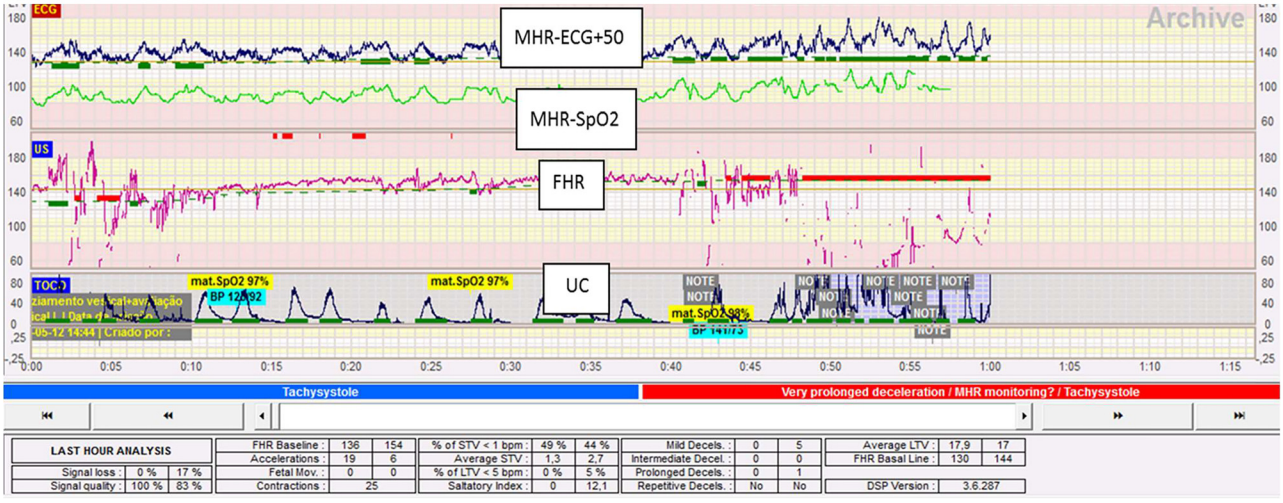


Figure 1: Examples for peculiarities of the systems for computerized analysis of cardiotocograms (cCTG) used in clinical practice.
Top: A cardiotocogram (CTG) during the last 45 min of a vaginal delivery; on the top is the fetal heart rate (FHR), in red; in the middle is an overlapping of the maternal heart rate (MHR) recorded with ECG (MHR-ECG), in dark blue, and the MHR recorded with oximetry (MHR-Oximetry), in green; on the bottom are the uterine contractions (UC), in black. Middle: The last hour of the top CTG with de SisPorto® analysis; on the top is the MHR-ECG analysis after the separation from the MHR-Oximetry by adding 50 bpm to the MHRECG recording (blue alarm-"Tachysystole"; results in the left columns of the "LAST HOUR ANALYSIS" on the bottom of the Figure); in the middle is the FHR analysis: Red-alarm-"very prolonged deceleration/MHR monitoring?/Tachysystole" (results in the right columns of the "LAST HOUR ANALYSIS" on the bottom of the Figure); on the bottom is the UC analysis. Bottom: The same analysis presented in the Midlle CTG after the removal of the MHR signals misrecorded as FHR; the FHR analysis changed (results in the right columns of the "LAST HOUR ANALYSIS" on the bottom of the Figure) and the alarm turned yellow-"Decelerations/MHR monitoring?/Tachysystole". MHR and FHR baselines are depicted as dotted green lines, accelerations as green bars and decelerations as red bars. For more explanations please see the text.

complexity than the patterns associated with calm sleep (pattern A) and wakefulness (pattern C) [45]. They also evidence that in fetuses with normal outcomes, from weeks 25–40 of gestational age, the mean FHR decreased significantly, whereas most variability indices increased; sympatho-vagal imbalance exhibited two local maxima at 29–30 and 34–35 weeks and decreased afterwards [46]. Additionally, Bernardes et al. evidenced that normal term female fetuses exhibited significantly more linear and significantly less complex FHR activity than their male counterparts, in the antepartum period [47]. They also showed that term female fetuses exhibited significantly more linear FHR activity than their female counterparts, while maintaining similar complex activity, in the final minutes of labor and when were born with acidosis [48] (Table 2).

Amorim-Costa et al. published reference charts for CTG parameters following the FIGO guidelines throughout normal pregnancy [49, 50]. From 24 to 41 weeks, the charts evidenced a decrease of FHR baseline and an increase of accelerations and variability; decelerations were practically zero for all gestational ages. FHR baselines were consistently higher in females whereas variability was lower [49, 50]. They also reported that during pregnancy the FHR baseline showed a more pronounced decrease in SGA fetuses, being higher at earlier gestational ages and lower later. Average LTV was significantly lower in SGA<p3 fetuses, but a parallel increase occurred in all groups. There was considerable inter-fetal variability within each group [51] (Table 3).

Studies on the influence of fetal presentation on FHR variability, maternal-fetal attachment [52] and twin-to-twin interactions [53, 54] were also published (Table 3).

Clinical studies

Table 1 summarizes the main systematic reviews about the present state of CTG analysis and cCTG in clinical practice [4, 5, 19, 20, 55, 56] and Table 4 summarizes the most representative clinical studies performed with the SisPorto® system for cCTG [52, 57–67].

Most clinical studies on cCTG, namely those performed with the SisPorto® system, are small validity case series studies, pertaining to the detection of compromised fetuses in high-risk pregnancies, during the antepartum period [57–61], or the to the detection of fetal hypoxia or low Apgar scores, during the intrapartum period [52, 62–65]. Some clinical studies are cohort studies or RCT, but only a minority of them has included a large number of cases [66, 67] or was included in meta-analysis studies [4, 5, 19, 20, 55, 56].

The main clinical study performed in the antepartum period with the SisPorto® system was published by Ayres-de-Campos et al. [59] Three hundred forty five CTGs were acquired in the same number of fetuses, from eight tertiary care centers in Europe and Australia, 4 h before an elective cesarean section. The receiver-operator curve (auROC) regarding the prediction of the 1 and 5 min Apgar scores under 5 and 7 were, respectively, 0.96–1.00 and 0.81–0.89, considering the different CTG variables, whereas the best auROC regarding the prediction of an UAB pH<7.15 was 0.69 [59] (Table 4).

The main clinical studies performed in the intrapartum period with the SisPorto® system were published by Nunes et al. [66] and Lopes-Pereira et al. [68]. Nunes et al. published a RCT that has involved 7,735 cases from five hospitals in the United Kingdom, pertaining to singleton, vertex fetuses of 36 weeks of gestation or greater during labor [66]. The cases were randomized to continuous central fetal monitoring by cCTG and online alerts (experimental arm) or visual analysis of CTGs (control arm). There were 16 cases of metabolic acidosis (0.40%) in the experimental arm and 22 (0.58%) in the control arm (relative risk 0.69 [0.36–1.31]) with no statistically significant differences found in the incidence of secondary outcomes. Computer analysis with real-time alerts did not significantly reduce the rate of metabolic acidosis or obstetric intervention. A lower-than-expected rate of newborn metabolic acidosis was observed in both arms of the trial [66]. On the other hand, Lopes-Pereira et al. compared two cohorts, one with 8,791 cases and the other with 29,675 cases, obtained, respectively, before and after the introduction in the clinical practice of a tertiary care hospital of the Ominiview-SisPorto® system with cCTG and ST analysis. The system was associated with significant reductions in hypoxic-ischemic encephalopathy and cesarean deliveries [68].

Discussion

In this paper the why, what and how of cCTG in clinical practice was illustrated with the experience obtained with the development of the SisPorto® system, thirty-two years after the publication of the first paper, issued in an indexed peer reviewed journal, that has presented the first version of the system [6]. The elaboration of a narrative review, with details related to the development of the SisPorto® system for cCTG, presented by one of its developers has a risk of overestimation of the results achieved with the system. However, this is the only way of presenting an experienced view about details related with the development of cCTG. As a form of guaranteeing the wider scrutiny possible about the paper, in this review only peer reviewed papers were included.

This paper shows that cCTG in clinical practice and the SisPorto® system are established research and clinical tools, with a relevant number of publications, including RCTs considered in meta-analysis studies [4, 5, 55, 56]. It is more difficult to obtain published information about other systems for cCTG in clinical practice, but there are definitely other systems that have also led to relevant publications. The 2CTG System® [68, 69], the Guardian + INFANT® (K2 Medical Systems, Plymouth, UK) [70, 71] and a system evaluated by Ignatov et al. [72] were also tested in RCTs that were included in meta-analysis studies [4, 5, 55, 56]. More information about other commercialized systems for cCTG in clinical practice may also be obtained in a review study published by Nunes et al. [73], namely the ARGUS® (GMT, Frankfurt, Germany) [73], the OB TraceVue system® (Philips Healthcare, Einthoven, The Netherlands [74], the OBIX Perinatal Data System® (Clinical computer systems Inc., IL, USA) [73], the PeriCALM system® (LMS Medical Systems, Montreal, Canada and PeriGen, Princeton, USA) [75, 76] and the Trium CTG Online® (Trium Analysis Online GmbH, Munich, Germany) [77].

A long way has been already travelled by cCTG in clinical practice but there still a long way to go. Overall, there is evidence that cCTG is superior to conventional CTG as it may save time spent in hospital for women, in the antepartum period, and is objective with at least equivalent results in maternal and perinatal outcomes, both in the ante and intrapartum periods [4, 5, 55, 56]. However, improvement of the mobility of the hardware with more wireless solutions is warranted, including the use of mobile phones. Cardiotocographic sensors also still need to be improved as to get CTG signals with less signal loss and noise. Pre-processing and processing algorithms have also a large room for improvement and artificial intelligence methods combining CTG and clinical data have only been developed in preliminary studies. Moreover, large clinical studies are still needed, not only in the antepartum and intrapartum clinical settings, where they have already been performed, with initial results, but also in other clinical settings, namely in twin pregnancies or FHR monitoring during premature labor.

Many research centers have now big CTG and clinical data [67, 78]. They have already published studies with huge numbers of cases [67, 78] while they keep using cCTG in routine clinical practice 24 h a day producing thousands of CTGs every year. Researchers have also started to share accumulated clinical and CTG data amplifying the possibilities of making research [79]. It is time to go on with further technical studies and larger studies in a wider range of clinical settings.

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