Computerized fetal cardiotocography analysis in early preterm fetal growth restriction - a quantitative comparison of two applications

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Published in:
Journal of Perinatal Medicine

DOI:
10.1515/jpm-2018-0412

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https://doi.org/10.1515/jpm-2018-0412
Received December 10, 2018; accepted February 8, 2019; previously published online April 22, 2019

Abstract

Background: We developed an open-source software for the computerized analysis of antenatal fetal cardiotocography (CTG) without limitation of duration of the registration, enabling batch processing and adaptation to any digital storage system.
Methods: STVcalc was developed based on literature about the FetalCare system (Huntleigh Healthcare Ltd, Cardiff, UK). For comparison with FetalCare, we selected the CTGs of all women who delivered in 2011 a small-for-gestational-age (SGA) fetus between 24 and 31 weeks by cesarean section (CS) for fetal distress, or had fetal death, before labor onset.
Results: In 471 CTGs from 39 women, the agreement was 99% for a short-term variation (STV) cut-off of 2.6 ms below 29 weeks and 3.0 ms thereafter, and 95% for 3.5 and 4.0 ms, respectively. In 18 (4%) cases, the proportional difference in STV between FetalCare and STVcalc was more than 10%.
Conclusion: As only slight differences were observed between the proposed feature-rich application and the FetalCare system, it can be considered valuable for clinical practice and research purposes.

Keywords: fetal cardiotocography; fetal growth restriction; fetal heart rate; short-term variation.

Introduction

Inter-observer agreement of the visual assessment of fetal cardiotocography (CTG) is suboptimal and no clear evidence exists for the use of antenatal CTG to improve perinatal outcome [1, 2]. Computerized cardiotocography (cCTG) analysis was developed nearly 40 years ago by Dawes et al. with the intention to improve antenatal fetal assessment [3].

Several commercial systems for cCTG analysis are available (Infant Guardian, K2 medical systems, Plymouth, UK; Omniview-Sisporto, Speculum, Alfragide, Portugal; FetalCare, Huntleigh Healthcare Ltd, Cardiff, UK). Also, a number of non-commercial systems have been described [4–7]. All the systems follow different algorithms and will therefore give different measurement results. For clinical antepartum cCTG analysis, we prefer FetalCare because the number of clinical studies using the FetalCare system is much larger than for other systems and only for the FetalCare system, clinically useful cut-off values have been described [8–20].

However, for research purposes, the FetalCare software has some disadvantages, as the analysis time is restricted to 1 h and batch processing is not available. Furthermore, when using FetalCare, we incidentally saw that an unexpectedly high STV was calculated in cCTGs with irregular spikes and signal loss. FetalCare only works with its own data acquisition and storage system. Centers that use a different digital storage system cannot use FetalCare, unless they design a conversion application, which is not commercially available.

To overcome these disadvantages, we developed a new software for short-term variation (STV) calculation (STVcalc). In this study, we describe and evaluate the algorithms which are used in our software. We investigated, using a set of cCTGs, the agreement between the proposed software and the FetalCare system, as this is currently the best described software for clinical antepartum cCTG analysis.

Materials and methods

Summary of the software design of STVcalc

The program for STV calculation was written in Python version 3.6 (Python software foundation) using the literature by Dawes

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[3, 21–24]. Two later publications were consulted additionally [12, 25]. We intended to follow the methods used by Dawes, but particular details for baseline construction could not be determined from the published literature.

CTGs were registered using Philips series 50A or M1350A machines (Philips Healthcare, Amsterdam, The Netherlands). These machines export fetal heart rate (FHR) values with a frequency of 4 Hz. The inter-beat interval (IBI = FHR/60,000 ms) was calculated from FHR, and the IBI was averaged over epochs of 3.75 s (16 epochs per minute). All further calculations were performed with epoch values. The procedure for cCTG analysis is summarized here – the complete description is available as supplementary information on the journal's website.

Baseline calculation consists of four intermediate steps. First, a reference value is calculated that is used to set constraints for the baseline calculation. Then an initial baseline level is calculated. Starting with this initial baseline level, the baseline continues using the average of the IBI values that are within the constraints in a moving window of 1 min duration. Lastly, the baseline is filtered to smoothen the baseline.

Following baseline calculation, all epochs with an IBI that differed more than 75 ms from the baseline (upward or downward) were marked as outliers. Decelerations were defined by periods of 60 s or more with an FHR below the baseline and a large difference from the baseline of more than 10 beats per minute (bpm), or of 30 s or more with a large deviation of more than 20 bpm. Accelerations were defined by a period of 15 s or more with an FHR above the baseline and a peak value at least more than 10 bpm above the baseline. For the definition of decelerations and accelerations, we followed the definitions used by Dawes for FetalCare [12, 24].

Outlier epochs that were not part of an acceleration or deceleration were, together with a neighboring epoch on each side, excluded from further calculations.

STV was calculated for each minute by averaging the absolute difference in the IBI of consecutive epochs. If a minute contained less than 50% valid epochs or if it was part of a deceleration, then this minute was excluded.

Long-term variation (LTV) was calculated for each minute by the addition of the largest deviation of IBI above the baseline to the largest deviation of IBI below the baseline within a minute, excluding minutes with decelerations. The minute values were averaged over the complete registration. An episode in which 5 of 6 consecutive minutes had an LTV of more than 31 ms was marked as "High variation", and if this was below 31 ms, it was marked as "Low variation".

Similar to FetalCare, a warning for a low frequency sinusoid pattern could be given if the STV/LTV ratio was very low. If this ratio was high, then an additional calculation was performed to test if the peak-to-peak and dip-to-dip intervals were mainly at 2–5 cycles/min.

Other characteristics of STVcalc

The CTG can be visually assessed and it is possible to exclude parts with an irregular signal or signal loss manually before heart rate analysis, or select periods of interest. It is possible to calculate a large number of CTG files in batch mode. There is no restriction on the duration of a CTG.

Currently, data can be read from binary files in the storage format used by the MOSOS CTG monitoring and archiving software (BMA Healthcare Solutions, Houten, The Netherlands), or from text files with one FHR value and one uterine pressure value per line, sampled at 4 Hz. For other binary formats, the data import module has to be adapted.

The software code of STVcalc is available from GitHub, a repository for freeware and host for collaborating not-for-profit software developers (https://github.com/hwolf46/STVcalc for Python source code and from https://github.com/hwolf46/STVexe for an executable program).

Study procedure

We included all women who delivered in 2011 in the Academic Medical Center, Amsterdam, The Netherlands, at a gestational age of 24–31 completed weeks with fetal death, or by cesarean section (CS) for fetal distress with a small-for-gestational-age (SGA) fetus, and who had at least two cCTGs recorded. SGA was defined by a birth weight below the 10th centile of a Dutch reference chart [26]. cCTGs were registered using Philips series 50A or M1350A machines (Philips Healthcare, Amsterdam, The Netherlands) and stored on a server using the MOSOS CTG monitoring and archiving software (BMA Healthcare Solutions, Houten, The Netherlands). During the study period, STV calculation was not used for clinical management.

The CTG recordings were formatted for use in FetalCare version 2.0 software (Huntleigh Healthcare Ltd, Cardiff, UK) and for STVcalc. Calculations of the same recordings were made with both the programs. As FetalCare only allows calculations over a CTG duration of 60 min, we also made calculations in STVcalc only over the first 60 min.

STV values calculated by FetalCare and STVcalc were compared as a continuous variable by the calculation of a proportional difference $[2\times(STV_{FetalCare} - STV_{STVcalc})/(STV_{FetalCare} + STV_{STVcalc})]$, but also after classification by two different STV cut-off levels that had been used in the Trial of Randomized Umbilical and Fetal Flow in Europe (TRUFFLE) study [19]. The higher cut-off level was set at 3.5 ms below the gestational age of 29 weeks, and at 4.0 ms at a longer gestational age, the lower cut-off level was set at 2.6 ms and 3.0 ms, respectively. Both the applications calculated the number of decelerations and accelerations over the first hour of registration. Additionally, one of the authors (HW) classified decelerations visually as variable when the interval and shape varied and as recurrent when decelerations occurred at regular intervals with similar shape. Registrations with a proportional difference between the STV calculated by FetalCare and by STVcalc of more than 10% were assessed visually in both the systems to determine a possible cause for the difference and assess differences in signal filtering between the applications.

Statistics

Values of STV, the proportional difference, and the number of decelerations or accelerations were compared by non-parametric tests as these values do not have a normal distribution. Data were presented as median with interquartile range (IQR).

Sample size calculation: to detect a difference of 5% between two measurements with a mean of approximately 5.0 and a standard deviation (SD) of 2.0, the sample size should be approximately 400 (alpha 0.05, beta 0.2). Statistical calculations were performed using IBM SPSS software version 25 (IBM, New York, NY, USA).

Ethics

The Medical Ethics Committee approval was not needed because this was a strictly anonymous cohort analysis using data stored in the department's database, without any direct relation to medical management or patients' interests.

Results

From the electronic patient data management system of the department, 135 women with a singleton pregnancy were selected, who delivered in 2011 at a gestational age of 24–31 weeks. Three women with infants with congenital abnormalities, 77 with preterm labor, preterm rupture of membranes or antepartum hemorrhage, and 16 with insufficient cCTG data were excluded because there was no intention to intervene on fetal distress due to low birth weight or gestational age (n = 6) or a short interval between admission and delivery (n = 10). The remaining 39 women met the inclusion criteria specified in the Methods section (Table 1).

The median gestational age at hospital admission was 27 weeks and that at delivery was 29 weeks, with a median birth weight of 920 g. Two fetal deaths were observed. In both the cases, it was decided, after discussion with the parents, to abstain from intervention due to an expected poor outcome based on gestational age and estimated fetal weight. In one of these cases, the STV over the first hour was 2.7 ms 12 h before fetal death (both applications), but 2.2 ms over the full length of 140 min with STVcalc, with repeated variable decelerations. In the other case, the STV was 2.6 ms (FetalCare) or 2.5 ms (STVcalc), with a solitary variable deceleration confirmed 18 h before fetal death. The two stillborn babies were delivered vaginally and all the others by CS. In one woman, the indication for CS was severe preeclampsia with moderate CTG abnormality. In all the others, the indication was based on an estimate of the fetal condition by the use of Doppler and visual assessment of the CTG, taking the gestational age into account. CTGs with low variability and/or decelerations were often not followed by CS because a next CTG after several hours appeared better.

The included 39 women had 496 CTG recordings (12.7 on average per woman). Usually, CTGs were performed twice daily, sometimes more often to confirm if an abnormal tracing was persistent. Twenty-five CTGs (5%) with insufficient lengths of less than 20 min or more than 50% signal loss were excluded. The remaining 471 CTGs had a median valid duration of 53 min (minimum 20 min, maximum 60 min).

Figure 1 shows a plot of STV values by FetalCare versus STVcalc. STV calculated by STVcalc was slightly lower than by FetalCare, with a median proportional difference of 0.02 (IQR – 0.01 to 0.05) (Table 2). This difference resulted in a slightly higher abnormal classification of CTGs by STVcalc, using STV criteria from the TRUFFLE study, although the agreement was high (95% and 99%,

Table 1: Obstetric and neonatal data of the study population.

n	39
Nulliparity	24 (62%)
Gestational age at inclusion, weeks	27 (25–28)
Preeclampsia	27 (69%)
Antihypertensive medication	29 (74%)
Umbilical artery PI	1.96 (1.58–2.56)
Umbilical/middle cerebral PI ratio	1.58 (1.03–1.90)
Placental abruption/bleeding before CS	6 (15%)
Fetal death	2 (5%)
Gestational age at delivery, weeks	29 (28–30)
Mode of delivery	
Vaginal	2 (5%)
CS before labor	37 (95%)
Indication for CS	
Fetal condition	36 (98%)
Maternal + fetal condition	1 (2%)
Birth weight	920 (730–1050)
Birth weight <p10	36 (92%)
Apgar 5 min. <7	4 (10%)
Neonatal morbidity	
Cerebral US abnormal (ICH/PVL)	0
Bronchopulmonary disease	5 (13%)
Sepsis/NEC	7 (18%)
Neonatal death <4 weeks	4 (10%)
Cause of neonatal death	2 NEC, 1 sepsis, 1 lung hemorrhage
Infant death 2–12 month	1 (2%)
Number of CTG	496 (average 12.7/woman)
Insufficient length (<20′) or signal loss >50%	25 (5%)
Number of CTG for evaluation	471
Decelerations (visually assessed)	
Variable 1–2/h	231 (49%)
Variable >= 3/h	34 (7%)
Recurrent	5 (1%)

CS, cesarean section; CTG, cardiotocography; ICH, intracerebral hemorrhage; NEC, necrotizing enterocolitis; PI, pulsatility index; PVL, periventricular leukomalacia; US, ultrasound.

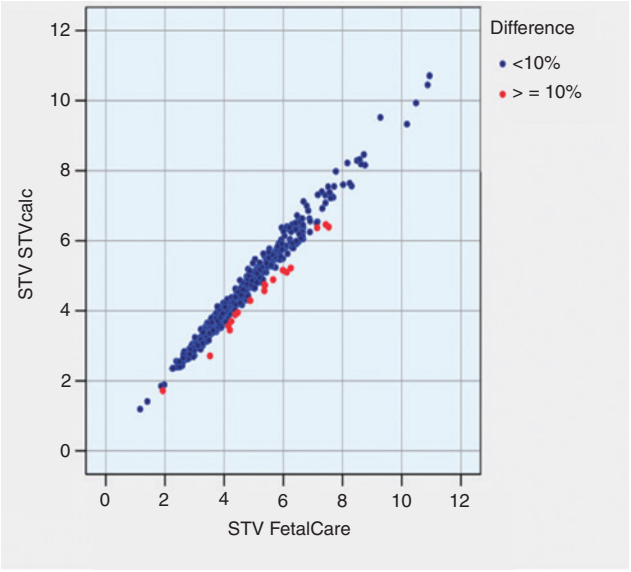

Figure 1: Scatterplot of STV by FetalCare and STVcalc.
In 453 values, the proportional difference between both was <10% (blue), and in 18 (4%) values it was ≥10% (red).

respectively for the higher and lower STV cut-off – Table 2). For the 23 (5%) CTGs with disagreement for the high cut-off, the STV values by both applications were close and the variation was small [FetalCare STV 3.7 (IQR 3.5 to 4.1) ms; STVcalc STV 3.7 (IQR 3.5 to 4.1) ms]. In 15 of these 23 cCTGs, STVcalc had a value below this cut-off, while FetalCare gave a higher value. In eight CTGs, the opposite was observed. All three cases that showed a disagreement for the low cut-off had a value below the cut-off by STVcalc [FetalCare STV 3.1 (IQR 2.8 to 3.3) ms; STVcalc STV 2.7 (IQR 2.7 to 2.8)].

The number of decelerations detected by STVcalc was higher than by FetalCare, while the number of detected accelerations was similar (Table 2). By visual assessment, decelerations were classified as recurrent in five (1%) and as variable in 265 (56%); in 34 (7%) of these, the deceleration frequency was three or more per hour. Comparison of the deceleration count of FetalCare and STVcalc with visual assessment showed a sensitivity and specificity of 79% and 81%, respectively, for FetalCare, and 94% and 59%, respectively, for STVcalc (Table 2).

In 18 (4%) of the CTGs, the proportional difference in STV between FetalCare and STVcalc was more than 10% (Figure 1). In all these cases, the STV by STVcalc was lower than by FetalCare. They were equally dispersed over the total range of STV values. Evaluation of these CTGs showed that the two applications differed in processing signal loss and downward spikes, which are quite common in cCTGs in early preterm fetal growth restriction. Furthermore, the applications had small differences in the baseline position, which affected the classification of decelerations. The main reason that STVcalc calculated a lower STV in these 18 cCTGs was the higher sensitivity for decelerations and a more sensitive exclusion of signal irregularities. Both signal irregularity and decelerations can contribute to an elevation of STV when not excluded from calculation. These differences between Fetalcare and STVcalc are demonstrated later in a number of cCTGs with a difference in STV of more than 10%.

Figure 2 demonstrates the effect of signal loss. FetalCare calculated STV at more than 6 ms during the first 15 min with signal loss, but 3.6 ms over the complete first hour. STVcalc calculated STV at 2.9 ms over the same CTG part, but at 2.4 ms over the complete CTG of 140 min. FetalCare had a similar result (2.4 ms) calculated over the period of 60–120 min. It seems, therefore, that the higher

Table 2: Comparison of FetalCare and STVcalc. Values as median (IQR), number (percentage) or percentage (95% confidence limits).

	FetalCare	STVcalc	Agreement
FHR, bpm	142 (136–148)	142 (136–147)	
STV[a], ms	4.6 (3.7–5.6)	4.4 (3.7–5.5)	
Proportional difference of STV[b]		0.02 (−0.01–0.05)	
STV <3.5/4.0 ms[c]	115 (24%)	122 (26%)	95% (93%–97%)
STV <2.6/3.0 ms[c]	21 (5%)	24 (5%)	99% (98%–100%)
Accelerations per CTG	1 (0–2)	1 (0–2)	79% (75%–82%)
Decelerations per CTG[a]	1 (0–1)	1 (0–2)	72% (68%–76%)
Sensitivity compared to visual assessment	79% (74%–83%)	94% (91%–97%)	
Specificity compared to visual assessment	81% (76%–87%)	59% (52%–66%)	

[a]Difference significantly different from 0 ($P < 0.001$; Wilcoxon signed rank test). [b]Proportional difference: 2 × (FetalCare – STVcalc)/(FetalCare + STVcalc), significantly different from 0 ($P < 0.001$; Wilcoxon signed rank test). [c]First cut-off value at gestational age <29 weeks, second one at >= 29 weeks gestational age. CTG, cardiotocography; FHR, fetal heart rate; STV, short-term variation.

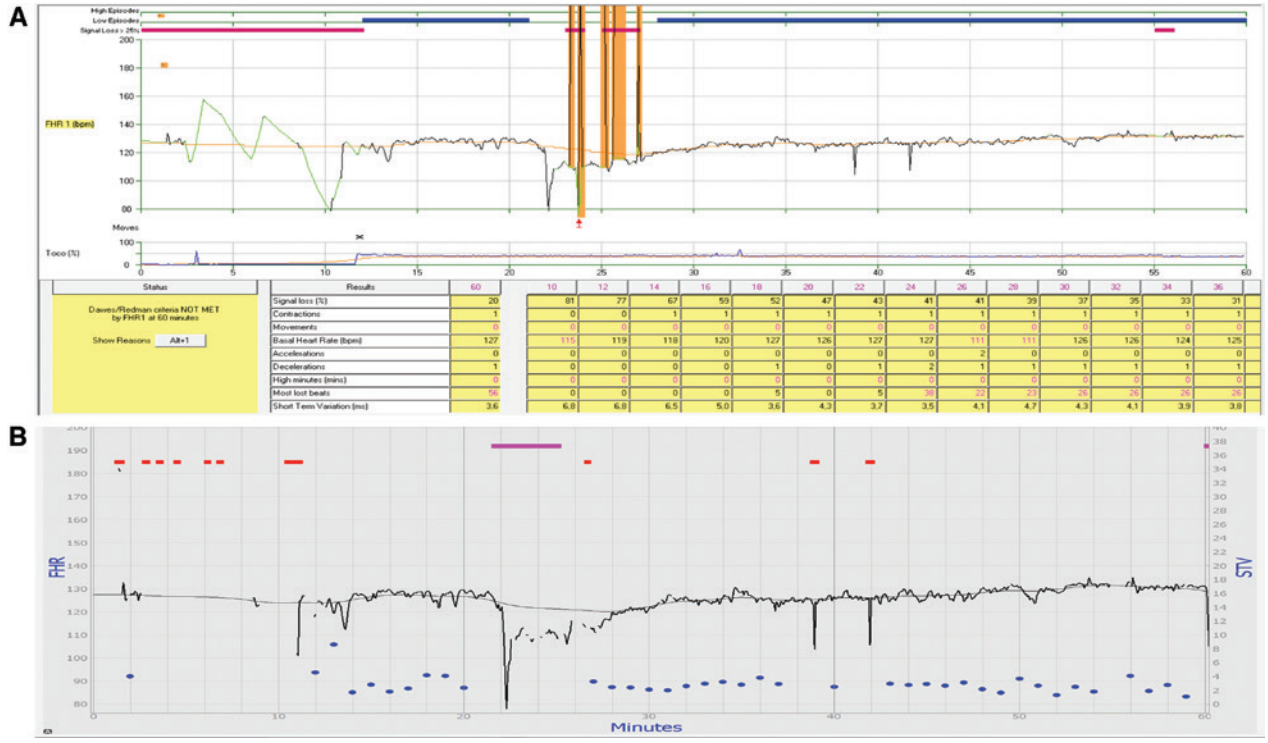

Figure 2: Cardiotocography tracing by FetalCare in panel A, and by STVcalc in panel B.
(A) FetalCare: STV of 3.6 ms over 60 min registration, but during the first 15 min with signal loss, the STV was more than 6 ms (see the yellow table with results after 60 min next to the Results items column and to the right of this, the results for each 2 min of the registration). STV over 60–120 min (not shown) was 2.4 ms. (B) STVcalc: STV of 2.9 ms over 60 min with one deceleration (top horizontal bar), after the exclusion of signal loss and downward spikes (second layer horizontal bars). The STV of each minute of the registration is shown by dots with a scale on the right. The STV of the complete CTG (140 min) was 2.4 ms. Case description: Para 0, referred at 26 + 3 for chronic hypertension and severe preeclampsia. Current CTG at 27.0, after which a caesarean section was performed: male, 700 g, respiratory distress syndrome (RDS) and bronchopulmonary dysplasia (BPD).

value of the first hour in FetalCare is wrongly influenced by signal loss during the first 15 min.

Figure 3 shows that FetalCare deals differently with outliers compared to STVcalc. Although the CTG pattern looks extremely flat, FetalCare calculates an STV of 6.1 ms. STVcalc excludes the outliers and calculates an STV of 3.4 ms. By visual assessment of the cCTG graph, which shows very little variation, the lower value seems more appropriate.

Figure 4 demonstrates how differences in deceleration classification can affect STV calculation. FetalCare calculates STV at 5.3 ms and counts no decelerations, while STVcalc marks two decelerations and excludes several outliers from the STV calculation, resulting in an STV of 4.7 ms.

In another cCTG with a flat pattern (not shown) and one downward spike to 85/min at 53 min, FetalCare calculated STV at 4.5 ms over the first 60 min and STVcalc at 2.7 ms. However, after the exclusion of the downward spike from the calculation, the STV by FetalCare was 2.8 ms.

All 18 cCTGs with a difference of more than 10% between STVcalc and FetalCare had similar problems with outliers and decelerations.

Both applications may have difficulty in recognizing decelerations and accelerations in highly variable CTGs because then the baseline may be pulled upward by the many accelerations.

Discussion

This study shows that two STV calculation software programs, using similar algorithms, have comparable results. There were small differences, caused by small differences in baseline calculation and exclusion of outliers or signal irregularities. We could not derive the method used by FetalCare exactly from the published literature. Therefore, we used what was published on the method and completed the baseline calculation with our

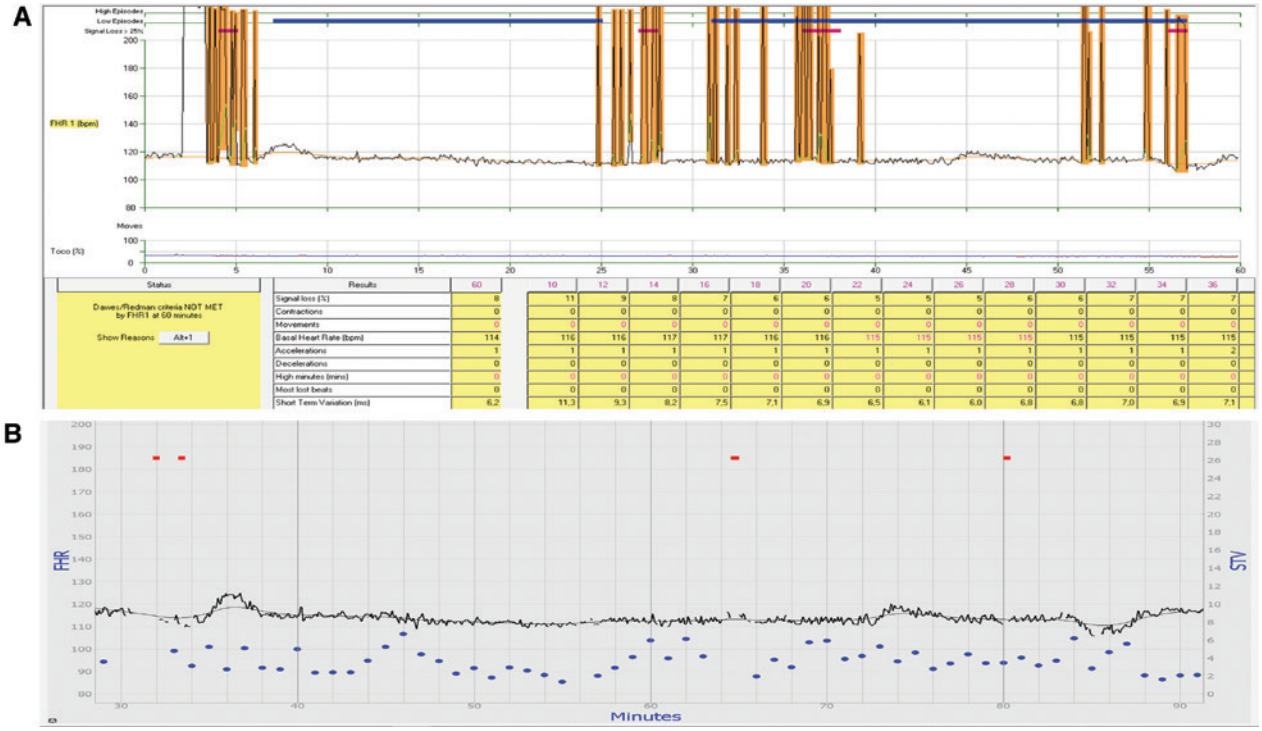

Figure 3: Cardiotocography tracing by FetalCare in panel A, and by STVcalc in panel B.
(A) FetalCare STV of 6.2 ms over 60 min. Very flat pattern with spikes. Note the very high early STV values in the bottom row of the yellow table below the graph. (B) STVcalc filtered out the signal loss in the beginning and the spikes (small horizontal bars above graph) and calculated STV of 3.4 ms. Case description: Para 0, referred at 29 + 5 weeks after eclampsia, stabilized with magnesium and antihypertensive treatment. Corticosteroids given. Current CTG at 29 + 6 weeks. Caesarean section for maternal and fetal condition 1 day later: female, 920 g, no severe neonatal complications.

own design. STV, decelerations and accelerations were defined exactly as published for FetalCare [3, 12, 21–24]. The agreement between both the applications for classification according to a gestational age-specific cut-off value of 3.5 or 4.0 ms was 95%. Only in a small minority of cases the decision making could be affected by differences, as in 15 CTGs (3%), STVcalc had a value below this cut-off, while FetalCare gave a higher value. In eight CTGs (2%), the opposite was observed. However, the absolute differences between these values were small. For the probably clinically more relevant low cut-off (2.6 ms or 3.0 ms), the agreement was 99%.

Overall, STVcalc gave slightly lower estimates for STV than FetalCare. STVcalc had a higher sensitivity for decelerations and excluded downward spikes more effectively. Decelerations and outliers often showed excessive signal variation, and could increase the STV if not excluded. This difference between both the applications can well explain the slightly lower STV with STVcalc compared to FetalCare. Dawes and Pardey described that short episodes of increases or decreases from the baseline of more than 75 ms are excluded in FetalCare, but on inspection of CTG registrations in FetalCare, this seems not to be affected [12, 24].

It is not possible to determine which software program could result in a better outcome as there was no association between STV classification and short-term outcome by either program. This is in line with a review that assessed the association of STV with acidemia at birth in women with fetal growth restriction. This review included 377 cases from four studies with fetal growth restriction and calculated that STV had a pooled positive likelihood ratio of 2.6 (1.6–4.0) and a negative likelihood ratio of 0.5 (0.3–0.8) for acidosis at birth [27]. Another study targeted at early preterm fetal growth restriction observed a non-significant relative risk for acidosis after a low STV of 1.4 [95% confidence interval (CI) 0.6–3.2, n = 387] [28]. These test characteristics are insufficient for reliable clinical discrimination.

Our study population was highly selective and far from normal. We decided not to use a normal population as it is of little interest to compare the STV values only of normal CTGs – the exact STV is irrelevant for clinical management if an STV is over 5 ms. However, around the

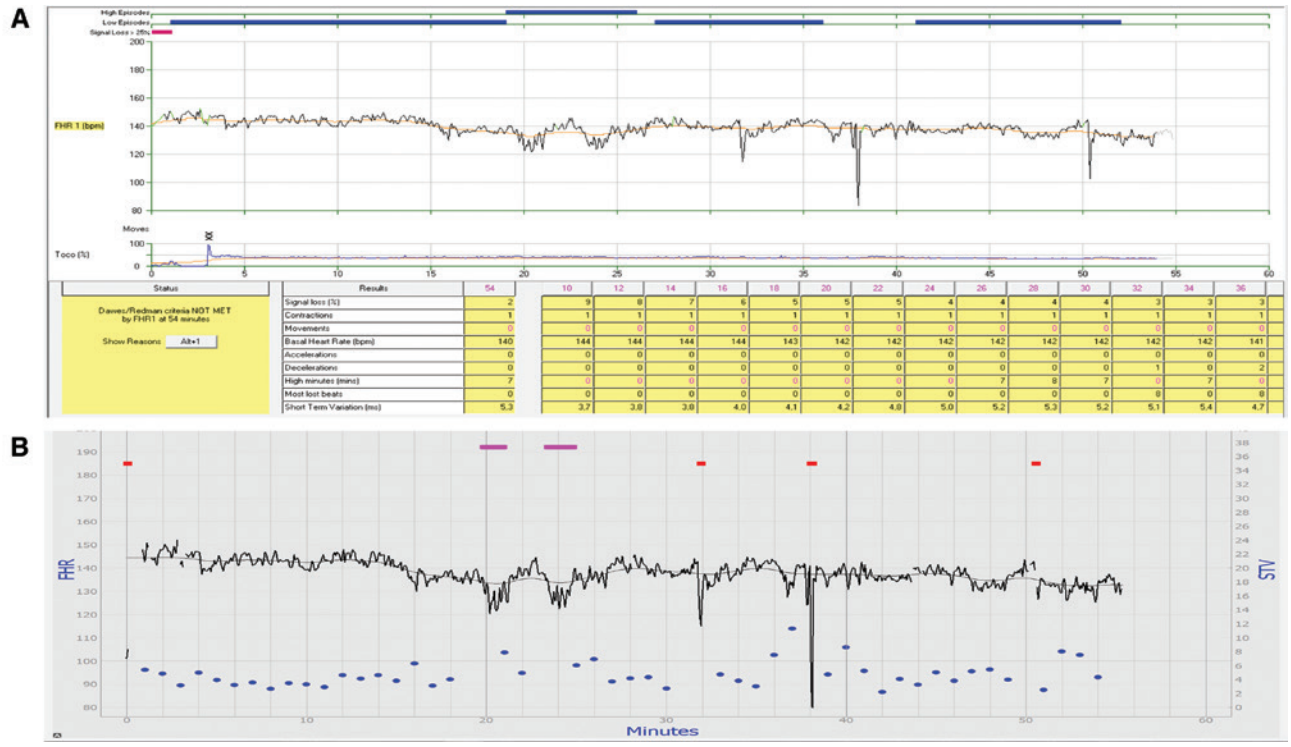

Figure 4: Cardiotocography tracing by FetalCare in panel A, and by STVcalc in panel B.
(A) FetalCare estimated STV at 5.3 ms over 60 min, the shallow decelerations at 20 and 23 min were not marked. (B) STVcalc estimated STV at 4.7 ms over 60 min with two decelerations (top horizontal bars), and downward spikes excluded (second layer horizontal bars). Case description: Para 0, admitted at 23 weeks for severe preeclampsia with preexisting renal insufficiency. Current CTG at 29 + 5 weeks. Caesarean section 1 day later for recurrent decelerations: female, 820 g, no serious neonatal complications.

cut-off levels, differences in estimation may be clinically relevant. Even in our population, most of the STV values (75%) were in the normal range (>3.5 ms below 29 weeks and >4 ms thereafter), because we used all the available cCTGs.

In early preterm fetal growth restriction, generally the STV is lower than when fetal growth is normal [29]. Variable decelerations and downward spikes are frequent probably due to oligohydramnios. Signal loss may occur more often than in larger fetuses. It is important that STV software applications deal with these common difficulties appropriately. It seems that STVcalc excludes outliers more effectively than FetalCare. Regardless of the program used, it is important to observe a CTG visually as well to determine if the signal quality is sufficient for calculation and if calculation errors due to signal loss could be possible.

From this study, it is clear that neither FetalCare nor STVcalc are reliable for the detection of decelerations. Baseline calculation is extremely important in this respect and there is no gold standard for this, neither computationally nor visually. Also by visual assessment, differences in interpretation may occur. Clear errors of computation may occur in CTGs with many accelerations and in CTGs where the fetal signal is temporarily replaced by a maternal signal. These are better differentiated visually. As deceleration detection affects STV calculation, a visual assessment should always be performed in conjunction with computerized analysis.

FetalCare restricts analysis to 1 h. This is probably not an issue in normal pregnancies, especially after 36 weeks, when fetal activity is more structured. However, in fetal growth restriction remote from term, variability is usually low, and decelerations, outliers and signal loss are common. Here a more prolonged assessment seems useful. In practice, many CTGs in our study had a duration of 2 h, and overall STV was often lower in the second half as the signal was often unstable in the beginning of the registration.

Evidence that computerized CTG analysis is superior to visual assessment is not available [2]. Notwithstanding this, in research a clear advantage is the numerical outcome, which facilitates the analysis of study results better than a classification as normal/suspect/abnormal, hampered by observer bias. Before it can be advised for clinical use, a large randomized trial needs to be

performed to assess the effect of the introduction of cCTG and the efficacy of different cut-off levels. The population that we selected for this study, with early preterm fetal growth restriction, could benefit most from such a trial.

Conclusion

Both the applications have similar results. STVcalc could have an advantage for both clinical practice as well as research as it allows the analysis of CTGs with a duration longer than 1 h. Particular advantages for research are the feature of batch processing, the independence of commercial digital storage formats and the availability as freeware. STVcalc excludes signal irregularities and outliers more effectively. Trials testing the effect of cCTG on long-term infant outcomes are needed.

Author contributions: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission. The authors do not have a conflict of interests nor a financial dependency or relationship with this project. The software that was designed for this project is published as freeware (GitHub).
Research funding: None declared.
Employment or leadership: None declared.
Honorarium: None declared.
Competing interests: The funding organization(s) played no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the report for publication.

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Supplementary Material: The online version of this article offers supplementary material (https://doi.org/10.1515/jpm-2018-0412).