Title

Prediction of labor onset type: spontaneous vs induced; role of electrohysterography?.

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Financial support for the research

- Grant from the Conselleria d'Educació, Cultura i Esport, Generalitat Valenciana Conselleria (GV/2014/029).
    - Role: Financial support only.
- Grant from the Universitat Politècnica de Valencia (SP20120490) and by a VLC_Campus grant (Prematuro ID34).
- Grant from the Ministerio de Economía y Competitividad y del Fondo Europeo de Desarrollo Regional. DPI2015-68397-R (MINECO/FEDER Role: Financial support only.
- General Electric Healthcare

- o Role: Financial support only.

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Word Count

3483 words including Abstract

Abstract

BACKGROUND AND OBJECTIVE

Induction of labor (IOL) is a medical procedure used to initiate uterine contractions to achieve delivery. IOL entails medical risks and has a significant impact on both the mother's and newborn's well-being. The assistance provided by an automatic system to help distinguish patients that will achieve labor spontaneously from those that will need late-term IOL would help clinicians and mothers to take an informed decision about prolonging pregnancy. With this aim, we developed and evaluated predictive models using not only traditional obstetrical data but also electrophysiological parameters derived from the electrohysterogram (EHG).

METHODS

EHG recordings were made on singleton term pregnancies. A set of 10 temporal and spectral parameters was calculated to characterize EHG bursts and a further set of 6 common obstetrical parameters was also considered in the predictive models design. Different models were implemented based on single layer Support Vector Machines (SVM) and with aggregation of majority voting of SVM (double layer), to distinguish between the two groups: term spontaneous labor (≤41 weeks of gestation) and IOL late-term labor. The areas under the curve (AUC) of the models were compared.

RESULTS

The obstetrical and EHG parameters of the two groups did not show statistically significant differences. The best results of non-contextualized single input parameter SVM models were achieved by the Bishop Score (AUC=0.65) and GA at recording time (AUC=0.68) obstetrical parameters. The EHG parameter median frequency, when contextualized with the two obstetrical parameters improved these results, reaching AUC=0.76. Multiple input SVM obtained AUC=0.70 for all EHG parameters.

Aggregation of majority voting of SVM models using contextualized EHG parameters achieved the best result AUC=0.93.

CONCLUSIONS

Measuring the electrophysiological uterine condition by means of electrohysterographic recordings yielded a promising clinical decision support system for distinguishing patients that will spontaneously achieve active labor before the end of full term from those who will require late term IOL. The importance of considering these EHG measurements in the patient’s individual context was also shown by combining EHG parameters with obstetrical parameters. Clinicians considering elective labor induction would benefit from this technique.

KEYWORDS

Electrohysterogram, SVM, majority voting, labor management.

1 Introduction

Late-term pregnancies are those that extend beyond the 40 + 6 weeks of gestational age (GA) up to 41 GA + 6 weeks, and are associated with an increase in fetal and maternal morbidity and mortality[1]. Induction of labor (IOL) is used before labor begins spontaneously to incite uterine contractions during pregnancy [2]. Medical indications for IOL are usually given in clinical situations in which the benefits of expediting birth outweigh the risks of continuing the pregnancy, as could be the case in a late term pregnancy [3]. There is an increasing trend in the use of IOL; from 1990 to 2012 the ratio doubled in the United States [4] from 9.5% to 22.5%, at an estimated cost of $2 billion [4].

IOL is not without certain risks. It entails the possible consequences of excessive uterine activity: C-section (cesarean section), risk of postpartum hemorrhage, and adverse effects on the new-born such as fetal infection and respiratory distress syndrome [1]. Late term pregnancies also involve risks. A review of the GA of all live infants in the United States (1995 - 2005) [5] and the American College of Obstetricians and Gynecologists [6] related a rise in stillbirths, neonatal and perinatal deaths at 41 GA compared to early and full term labor. In this regard, prior knowledge of when a pregnancy will exceed the term period would be very useful extra information to help clinicians manage pregnancies, especially in conditions such as high-risk gestations, advanced maternal age or human-assisted reproductive technology gestations. Similarly, current international recommendations encourage mothers to make an informed decision about the management of their own prolonged pregnancies [7]. The lack of clear evidence on the outcome of each pregnancy management strategy complicates the mother's informed decision between the risks associated with a late-term pregnancy and the risks associated with IOL. We develop a method that helps to determine, in term pregnancies, if active labor will be spontaneously achieved before the end of full term (<41 GA [6]) or if the patient will have a prolonged gestation, becoming a late-term pregnancy requiring IOL. This method would have considerable benefits for obstetricians considering management strategies and help mothers take decisions.

Previous studies attempted to develop models based on ultrasound technologies that predict the labor onset type: spontaneous vs C-section [8] or predict spontaneous vaginal delivery [9]. Other authors have used the Bishop Score (BS) and other maternal or fetal parameters to predict failed induction [10] or time to onset of labor in prolonged pregnancies [11]. To date, these models have shown limited predictive accuracy. One of the alternatives now available is to use the information derived from electrohysterographic recordings. Surface recording of the electrohysterogram (EHG) is a noninvasive technique for monitoring the electrical activity of the myometrium and provides reliable information on uterine contractions [12]. These contractions are the result of bursts of myometrial electrical activity and are associated with an increase in the intrauterine pressure [13]. The uterine electrophysiological conditions are reflected in the characteristics of the EHG signal and their evolution along gestation[14]. A large number of studies have used EHG parameters and classification methods mainly to discriminate labor contractions from non-labor contractions [15], and term from preterm deliveries [14-16], and in a minor extent to study the effect of different drugs [17, 18] .Although results have shown great potential of EHG, so far clinical application is very limited. This is probably due to incommodities derived of some recording protocols and equipment’s used in research studies, and also because clinicians are not familiar with EHG signals, and physiological interpretation of some EHG parameters and analysis procedures could also complex and not straight forward. Usually temporal and spectral parameters are used to characterize EHG signals[14, 16, 19, 20], especially EHG contractions bursts. Some authors also include non-linear characteristics in the EHG study [21, 22]. There is also a recent trend on the study of coupling and propagation of EHG by means of multichannel recordings [23-25].

When characterizing the uterine electrophysiological condition during pregnancy and determining the possible labor onset, it should be considered that pregnancy is composed of two steps: preparatory (long conditioning) and active labor. In the myometrium, this preparatory process involves changes in the transduction mechanisms [26], and so the spectral and temporal EHG parameters exhibit a longitudinal evolution throughout pregnancy [27], i.e. they are GA-dependent. On the other hand, maternal age, body mass index (BMI), parity, and gestations also influence the pregnancy and labor processes underlying the changes of the uterine electrical activity during pregnancy. BMI and parity are good predictors of cervical ripening, whose goal is to facilitate the process of cervical softening, thinning and dilating [28]. Also, nullparity, advanced maternal age and obesity are known to be strong risk factors in late-term pregnancies [29]. Our hypothesis is therefore that when characterizing the uterine electrophysiological condition by means of EHG analysis, the EHG parameters cannot be fully explained and interpreted outside the maternal clinical context characterized by common obstetrical parameters.

In this study, a set of individual and aggregation of support vector machines (SVM) classifiers using EHG recordings and obstetrical parameters from term pregnancies was implemented and compared to discern patients that will achieve active labor spontaneously before the end of full term (<41 GA [6]) from those that will need late term IOL (between 41 weeks 0 days and 41 weeks 6 days [6]). We studied the influence of the set of input variables on the performance of the classifiers with single input and groups of i) obstetrical parameters only, ii) EHG parameters only and iii) the combination of EHG parameters and their obstetrical parameters (clinical context).

The experimental results showed that the classifier that uses as inputs the combination of contextualized EHG parameters in an aggregation of support vector machines with the majority voting method gave the best performance.

2 Material and Methods

2.1 Patients

This study was approved by the Hospital Universitario y Politécnico La Fe de Valencia Ethics Committee and adheres to the Declaration of Helsinki. All the patients involved signed written consent forms. Inclusion criteria were: healthy women, with singleton pregnancy, term GA, and non-high-risk pregnancies. Patients with previous C-section, elective cesarean, pregnancy complication either maternal or fetal, or those who delivered in a different hospital were excluded from the study. All the patients presented uterine dynamics when recorded and were followed up until the end of the delivery. In accordance with ACOG Guidelines Committee Opinion No 579: Definition of Term Pregnancy [6], each patient's recording was assigned to one of two following categories: those expected to achieve active labor spontaneously before the end of full term (<41 GA) and those expected to need late term.

Of the 72 pregnant patients who consented to participate in the study, 10 were excluded as their delivery was by elective caesarian section due to breech presentation. Of the 62 analyzed, 38 spontaneously entered into labor before the end of full term and 24 late term deliveries were induced by standard medical criteria.

2.2 Electrohysterography signal acquisition

For each recording session, the subject's abdominal surface was prepared with abrasive gel (Nuprep, Weaver and Company, USA). A bipolar signal was captured from two Ag/AgCl disposable electrodes (Kendal, USA) placed subumbilically (2.5 cm apart) in the median axis (Figure 1). The electrodes were connected to commercial biosignal amplifiers (ECG100C, Biopac, USA) in which the signals were amplified and filtered between [0.05, 35] Hz to be subsequently acquired at a sampling frequency of 500 Hz. Conventional pressure recordings on abdominal surface were also performed with a commercial maternal monitor Corometrics 250cx (General Electric Healhcare). All the recording sessions lasted 30 minutes.

To eliminate low- and high-frequency interference and noise, the signals were bandpass filtered between 0.2 – 1 Hz with a 5th order Butterworth filter and subsequently down-sampled at 20 Hz [30]. All the EHG bursts were then segmented manually according to the following rules: the EHG bursts had to correspond in time to the contractions detected in the simultaneous uterine pressure record, and no artifact evidence should have been observed during contraction [31]. Fig. 2 shows an example of EHG signals recorded simultaneously with TOCO during a period of contractile activity. It can be seen that a uterine contraction is associated with increased pressure in the TOCO recordings and with a spike burst containing a rise in amplitude and frequency in the bioelectrical signal (EHG recording).

2.3 Parameterization

Only EHG signals of the uterine contractions identified in the recordings (EHG burst) were used for the analysis. A set of spectral and temporal parameters described in previous studies [12, 32, 33] was created to characterize the EHG bursts, including: duration (DurCT), number of contractions in the recording session (nCT), mean frequency (MF), median frequency (mF), standard deviation of frequency (stdF), dominant frequency (DF), subband energies normalized with respect to the total energy (NE1: 0.2– 0.34 Hz, NE2: 0.34 – 1 Hz) [33], and subband power P1: 0.2 – 0.34 Hz, P2: 0.34 – 1 Hz.

The obstetrical parameters included were: maternal age, BMI, gestations, parity, Bishop Score and days of gestation at recording moment. Maternal age was defined as age in completed years at time of recording, parity as the number of previous births including abortions at 28 GA or later, and GA was determined by prenatal ultrasound [29]. The BS is a points system determined by cervix dilation, effacement, station of the fetus, consistency of the cervix and its position [34] as measured on the day of the recording session.

Significant differences between the two sample groups were tested with a t-test for each parameter, in which a two-sided p value less than 0.05 was considered to be statistically significant.

2.4 Feature selection

Automatic parameter selection was carried out to achieve the maximum classifier accuracy. The Sequential Forward Feature Selection (SFFS) algorithm was used to determine the parameter set that maximized classifier accuracy. This is a bottom-up search procedure in which one parameter is added at a time to the current parameter set. The new parameter added is selected from the subset of the remaining parameters with the aim of minimizing misclassification errors [35, 36].

2.5 Classifiers

A total of 33 classifiers were developed to predict spontaneous labor before the end of full term or IOL in late term (Figure 3). In order to determine the ability of each parameter to discriminate between these two groups, a first set of 16 SVM models were implemented using non-contextualized single input parameters ($NCSP_i$, i=1..16, i=1..6 for obstetrical parameters and i=7..16 for EHG parameters). Secondly, based on the idea that in medicine the patients' signs, symptoms or information should not be analyzed as independent parts but united and related parts of a whole biological system; we consider that each EHG parameter can be influenced/modulated by the patient's obstetrical parameters and cannot be fully explained and interpreted outside the maternal clinical context; i.e. more uterine electrophysiological information can be derived when considering possible interactions by joining together the information about myoelectrical activity from uterine muscle (EHG parameter) and that of cervix condition (Bishop score), number of previous labors or gestational age for example.

Moreover, this interaction can be different for different EHG parameters and could be better modeled for single EHG parameters rather than considering all parameters together (also tested later with multiple input parameters, $SLMP_3$). Hence, so as to complete patient anamnesis and to consider such possible interactions, a second set of 10 SVM models with contextualized single EHG input parameters (CSPj, j=1..10) were also implemented to assess the ability of each EHG contextualized parameter to discriminate between the two groups. The inputs of each of these SVM classifiers were one EHG parameter and two obstetrical parameters (BS and GA at time of recording) for the EHG parameter contextualization. In addition, 3 single-layer SVM models with multiple input parameter ($SLMP_k$, k=1..3) were calculated to be able to compare the classificatory performance when combining more than one input parameter: $SLMP_1$ with obstetrical parameter inputs only, $SLMP_2$ with EHG parameters only, and the $SLMP_3$ with both obstetrical parameters and EHG parameters in a global approach. Finally, with the aim of improving the ability to discriminate between the groups, 4 aggregations for SVM models with an additional layer that included a majority voting method were also tested. The inputs of these double layer multiple parameter SVM classifiers ($DLMP_l$, l=1..4) were the multiple outputs of previous single input classifiers – $DLMP_1$: obstetrical parameters (6 outputs from $NCSP_{1-6}$) – $DLMP_2$: EHG parameters (10 outputs from $NCSP_{7-16}$), $DLMP_3$: obstetrical parameters and EHG parameters (6+10 outputs of $NCSP_{1-16}$) and $DLMP_4$: contextualized EHG parameters (10 outputs of CSP_{1-10}).

2.6 Validation methods

The Holdout Cross-Validation [37] technique was used to minimize the generalization error. The training and test sets were selected randomly from the whole data set, 80% of the data was designated for training, and the remaining 20% for testing [38]. The learning and testing stages must be repeated, since the selection of the instances is random, so the average performance obtained from 50 trials was utilized to minimize bias [35].

The predictive performance of each classifier was evaluated using the Receiver Operator Curve (ROC), which is a standard technique of summarizing a classifier's performance based on displaying sensitivity against 1 – specificity [32].

3. Results

Table 1 shows the obstetrical parameters. There were no statistically significant differences for these parameters between the two groups (spontaneous ≤full term labor and IOL late term labor). Furthermore, as can be seen in Table 1, the GA at the time of recording for both groups were almost identical. Similar EHG parameters were also obtained for both groups (see Table 2), there were no statistically significant differences between the EHG parameters of the two groups.

Table 3 (non-contextualized column) summarizes the performance of the 16 SVM models with a single input. Neither the obstetrical nor EHG parameters achieve good results when used as single inputs. BS (AUC=0.65) and GA at recording (AUC=0.68) - from obstetrical parameters- are provide the best information to the decision model with the best results. As the AUC values from all the EHG parameters ranged between 0.46 and 0.58, we can consider that a single EHG input parameter does not provide enough information to satisfactorily discriminate between patients that will achieve spontaneous labor before the end of full term from those that will require late term labor induction.

Table 3 (contextualized column) summarizes the computation of an SVM model for each single EHG parameter contextualized with obstetrical parameters. Only BS and GA at recording were used for contextualization, since the addition of other obstetrical parameters did not improve the results. Contextualization significantly improves the classifiers' performance, with AUC values ranging from 0.69 (contextualized EHG number of contractions) up to 0.76 (contextualized EHG median frequency). This improvement could also be attributed to the fact that these classifiers have 3 input parameters (1 EHG and 2 obstetrical parameters). Further information on this issue can be deduced from the other set of classifiers.

Table 4 shows (single layer column) the results for SVM models with multiple input data. Three SVM models were calculated: one for obstetrical parameters, one for EHG parameters, and the last was a combination of all the previous parameters. The SVM model for multiple obstetrical parameters gave an AUC=0.69. The SVM model for multiple EHG parameters achieves similar results as the obstetrical SVM model, AUC=0.70. The combination of obstetrical parameters and EHG parameters gives an AUC=0.76. The parameters most frequently selected by the algorithm were: BS and GA at recording from the obstetrical parameters, and median frequency from the EHG parameters, which is consistent with the results obtained by contextualized single EHG parameter classifiers.

Finally, the right-hand column in Table 4 shows the results of the double-layer classifiers that include majority voting. The SVM aggregation for obstetrical parameters only (AUC=0.75) and EHG parameters only (AUC=0.77), and the combinations of these two sets (AUC=0.82) shows a slight improvement with respect to the SVM models with multiple inputs. The best performance was obtained aggregating the SVM models for contextualized EHG parameters (AUC=0.93). This shows that the possibility of generating a particularized contextualization transformation for each EHG parameter (instead of an overall one for all the EHG parameters, as in $SLMP_3$ and $DLMP_3$, which joined obstetrical and EHG parameters together), improves the characterization of the uterine electrophysiological condition and hence the classifier’s performance.

4. Discussion

In this study we developed and tested classifiers able to distinguish patients that will achieve labor spontaneously before the end of their full term from those that will require late term IOL. This information would help clinicians to better manage the final steps of high-risk pregnancies and to optimize the use of hospital resources such as labor wards. In the case of expected late term IOL, and if risks could increase with prolonged gestation, it could be decided to re-schedule IOL accordingly. This information would also help mothers to make an informed decision about the management of a possible prolonged pregnancy, since such decision not only affects the maternal and fetal wellbeing but also influences the satisfaction with the delivery experience.

Lots of studies have been published showing the great potential of EHG to help to predict labor in other important obstetrical context: prediction preterm vs term deliveries[19, 20, 23-25, 38-40]: Lucovnik et al[40]. showed significant differences of propagation velocity and power spectral peak for preterm patients delivering within 7 days of measurement vs those delivering more than 7 days from measurement; and obtained an AUC of 0.96 for EHG burst analysis and 0.72 for the Bishop score; similarly Fergus et al [38] using SVM and EHG parameters from 30 min windows (including basal activity) achieved an AUC=0.95 for preterm delivery prediction. However, as far as we know, no studies have yet been published specifically dealing with predicting the onset of spontaneous labor vs late term induction by means of EHG parameters. In contrast to preterm patients[40], in the present study no significant differences were found in EHG parameters of patients that achieved spontaneous labor to those that required IOL at late term. Our results showed that the electrophysiological parameters extracted from the EHG burst should be contextualized for individual patients, taking into account the obstetrical parameters to create a complete anamnesis. Specifically, the best performance was achieved by the contextualized EHG parameters in both the single-layer SVM models and aggregation SVM models with majority voting. The latter improves the prediction capability by up to AUC=0.93.

Other studies have used ultrasound methods to investigate the labor outcome. Rao et al [8] used a regression analysis combining cervical length and maternal characteristics to predict spontaneous labor achieving an AUC=0.76. Vankayalapati et al [9] used the sonographic assessment of cervical length to predict spontaneous onset of labor in a 6 to 10 day interval, obtaining an AUC=0.64. Strobel et al [11] used the BS and ultrasound assessment of the cervix to predict time to delivery in prolonged pregnancy, achieving good results when the time to labor/delivery was less than 24 h and 48h (AUC=0.94 and AUC=0.90, respectively). However, when labor/delivery was longer than 96h, the AUC dropped to 0.66. In the present study, an AUC of 0.93 was obtained being the average time interval from time of recording to delivery 120h in ≤full term and 168h in late term labor groups. Our results show that the combination of the BS, maternal GA and EHG parameters improves the predictive performance of classifiers that only use obstetrical parameters. We therefore consider that electrohysterography could provide very valuable information in this clinical context. Although segmentation of the EHG burst and its parameterization would require additional time and effort, clinicians should be given the tools for automatic segmentation and analysis of EHG recordings [19, 35] to facilitate their work.

Our study is not exempt from certain limitations: Firstly, so as to simplify recording protocol only one EHG bipolar signal was analyzed in each patient. Other authors propose multichannel recording with 16 and even 64 monopolar channels [24, 41, 42]. Such systems can provide more information, and also permit to compute bivariate signal parameters to value EHG signal propagation and coordination. Possible enhancement of classificatory results when including more channels and such parameters, at the cost of a more complex recording condition, and the use of non-linear parameters should be tested in future work. On the other hand only patients with uterine dynamics were included in the study. To enhance the clinical applicability of the proposed tool, it should be extended to patients who do not present uterine dynamics. It should also be highlighted that the recordings were carried out at term (37-41 GA). Although the results are promising and could have great clinical value, it would be interesting to analyze the prediction performance of the classifiers in an extended range of gestational ages, and also to test similar classifiers for the prediction of preterm labor. Finally the combination of complex machine learning methods can yield good results. However, when the EHG parameters do not have an immediate physiological interpretation clinicians may not be willing to accept these techniques. Despite these limitations, the results indicate that this is a promising method for use in clinical obstetrics.

5 Conclusions

Clinicians and expectant mothers should have access to the best available evidence when deciding whether to induce labor. We have shown that measurements of electrophysiological uterine condition by means of electrohysterographic recordings can yield a promising clinical decision support system for distinguishing patients that will spontaneously achieve active labor before the end of their full term from those who will require late term IOL. We have also shown the importance of considering these EHG measurements in the patient's individual context by combining EHG and obstetrical parameters. This procedure could also be expanded and tested in other obstetrical situations, such as preterm labor prediction. We consider that present work and further future steps along the same lines could provide new approaches in clinical praxis to improve obstetrical care.

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Tables

Table 1: Patient characteristics for ≤Full Term and Late Term labor groups.

Obstetrical parameters	≤Full term (n = 38)	Late term (n = 24)
Gestations	2.34 ± 1.36	2.08 ± 1.34
Parity	0.84 ± 1.02	0.54 ± 0.77
Bishop	2.42 ± 1.95	1.08 ± 1.34
Maternal age (y)	31.4 ± 6.2	32.3 ± 4.3
BMI (kg/m^2)	28.8 ± 4.6	28.6 ± 3.7
GA at recording (days)	277 ± 4	280 ± 5
GA at birth (days)*	282 ± 4	288 ± 2

* statistical differences ($p<0.05$)

Table 2: Mean ± SD values of EHG parameters for both ≤full term and late term labor groups.

EHG Parameters	≤Full term (n = 38)	Late term (n = 24)
Contraction duration (s)	85.2 ± 46.0	85.7 ± 34.1
Number of contractions in 30min	2.89 ± 2.45	2.25 ± 1.56
Mean frequency (Hz)	0.36 ± 0.67	0.38 ± 0.71
Median frequency (Hz)	0.33 ± 0.66	0.33 ± 0.61
Standard deviation frequency (Hz)	0.14 ± 0.35	0.15 ± 0.04
Dominant frequency (Hz)	0.32 ± 0.06	0.31 ± 0.04
Normalized Energy [0.2– 0 .34] Hz	0.57 ± 0.17	0.54 ± 0.20
Normalized Energy [0.34 - 1] Hz	0.42 ± 0.17	0.45 ± 0.20
Power [0.2 – 0.34] Hz	0.25 ± 0.68	0.26 ± 0.57
Power [0.34 - 1] Hz	0.09 ± 0.29	0.09 ± 0.22

Table 3: Area under the curve (AUC) of SVM models with single input parameters with and without using obstetrical parameters for contextualization (NCSP and CSP, respectively)

SVM Model	Non-contextualized (NCSP)	Contextualized (CSP)
Gestation	0.54	--
Parity	0.52	--
Bishop	0.65	--
Maternal Age	0.51	--
BMI	0.40	--
GA at recording	0.68	--
Contraction duration	0.47	0.72
Number of contractions	0.48	0.69
Mean frequency	0.58	0.72
Median Frequency	0.46	0.76
Standard deviation frequency	0.47	0.73
Power [0.2 – 0.34] Hz	0.49	0.70
Power [0.34 - 1] Hz	0.46	0.71
Normalized Energy [0.2 – 0.34] Hz	0.46	0.74
Normalized Energy [0.34 - 1] Hz	0.48	0.71
Dominant frequency	0.47	0.75

Table 4: The area under the curve (AUC) of SVM models with single layer and double layer (majority voting) with multiple parameters (SLMP) and (DLMP) for each data set.

SVM Model	Single layer (SLMP)	Majority voting (DLMP)
Obstetrical parameters	0.69	0.75
EHG parameters	0.70	0.77
Obstetrical parameters and EHG parameters	0.76	0.82
Contextualized EHG parameter	--	0.93

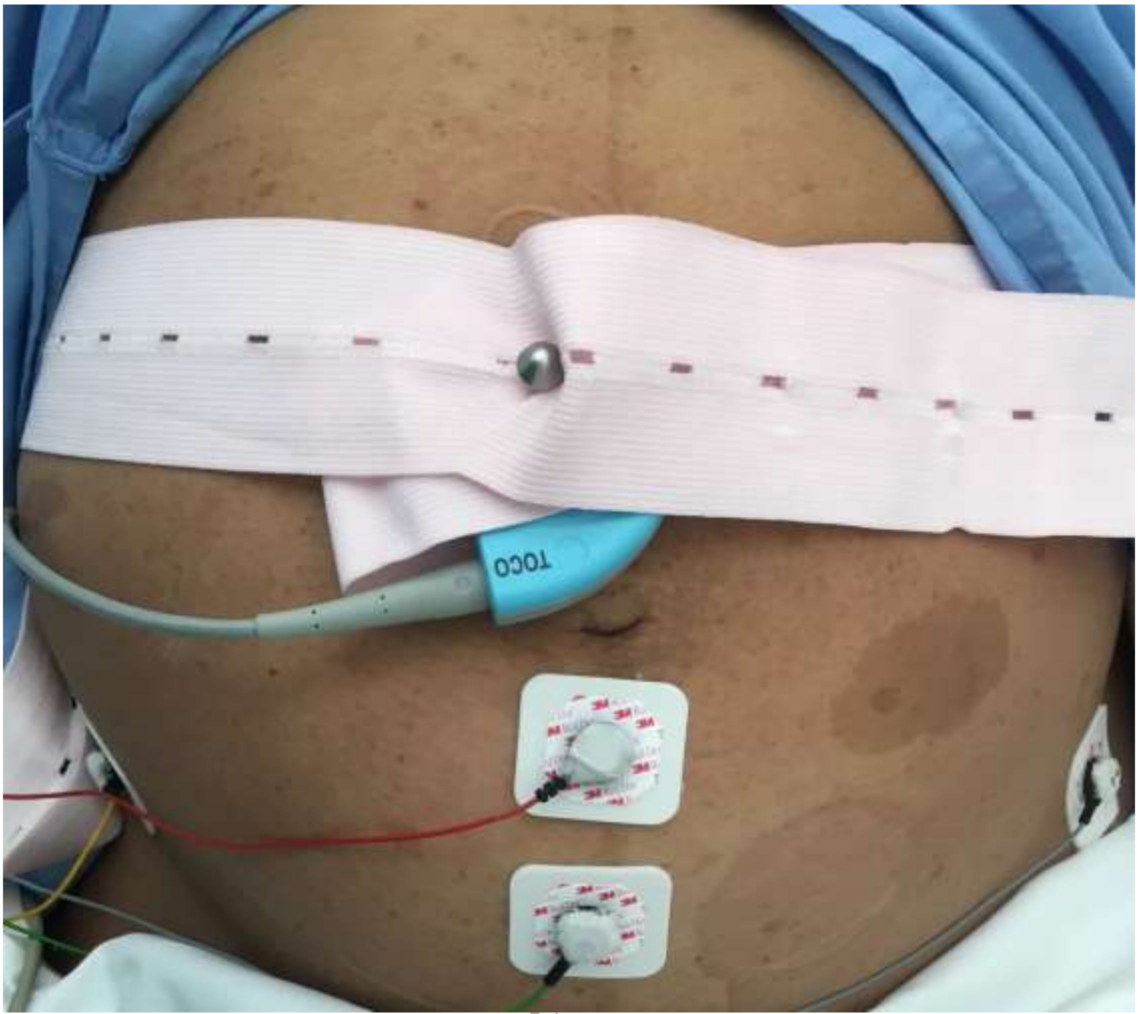

Figure 1: Electrode disposition in the experimental protocol

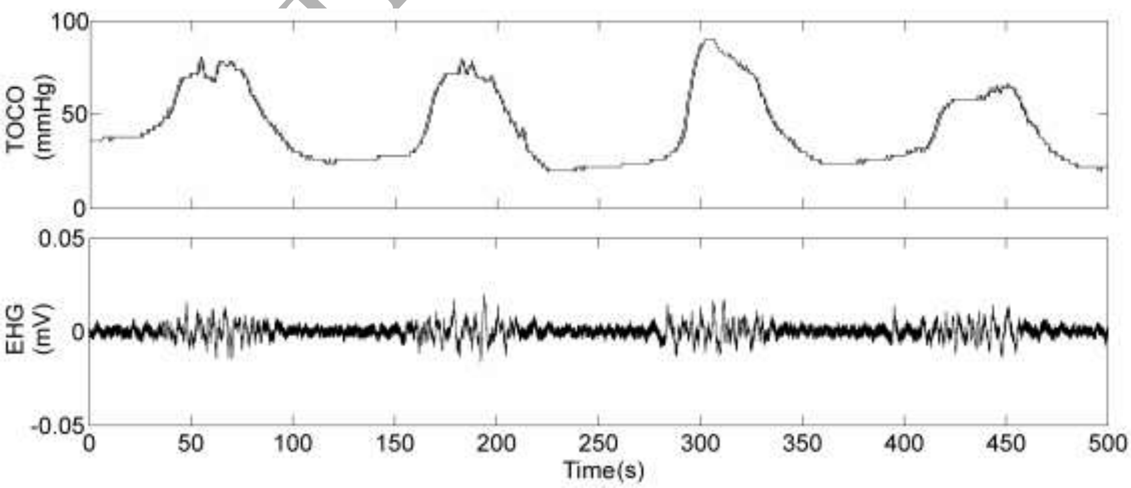

Figure 2: Abdominal surface recording during contractile period: TOCO signal (upper), and EHG signal (lower).

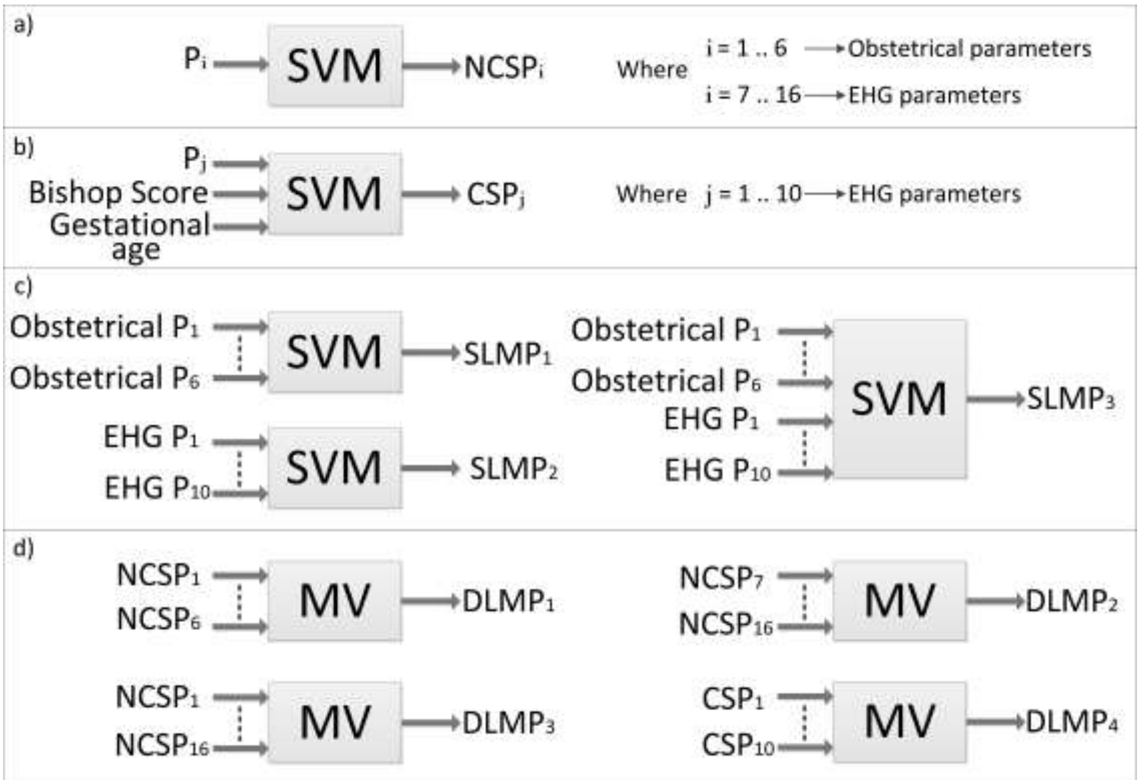

Figure 3: Classifiers developed to predict ≤full term spontaneous labor or IOL in late term pregnancies. SVM models depicted in descending order: a) 16 NCSP: non-contextualized single input (obstetrical and EHG) parameters (*P*), b) 10 CSP: contextualized single EHG input parameters with obstetrical parameters (Bishop Score and GA at recording) for contextualization, c) 3 SLMP: single layer with multiple input parameter, d) 4 DLMP: double layer (majority voting) with multiple input parameter.