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Assessing uterine electrophysiology prior to elective term induction of labor

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ABSTRACT

Objective: The purpose of this study was to determine if uterine electrophysiological signals gathered from 151 non-invasive biomagnetic sensors spread over the abdomen were associated with successful induction of labor (IOL).

Study design: Uterine magnetomyogram (MMG) signals were collected using the SARA (SQUID Array for Reproductive Assessment) device from 33 subjects between 37 and 42 weeks gestational age. The signals were post-processed, uterine contractile related MMG bursts were detected, and parameters in the time and frequency domain were extracted. The modified Bishop score calculated at admission was used to determine the method of IOL. Wilcoxon's rank-sum test was used to compare IOL successes and failures for differences in gestational age (GA), parity, modified Bishop's score, maximum oxytocin, and electrophysiological parameters extracted from MMG.

Results: The average parity was three times (3x) higher (1.53 versus 0.50; $p = 0.039$), and the average modified Bishop score was 2x higher (3.32 versus 1.63; $p = 0.032$) amongst IOL successes than failures, while the average GA and maximum oxytocin showed a small difference. For the MMG parameters, successful IOLs had, on average, 3.5x greater mean power during bursts (0.246 versus 0.070; $p = 0.034$) and approximately 1.2x greater mean number of bursts (2.05 versus 1.68; $p = 0.036$) compared to the failed IOLs, but non-significant differences were observed in mean peak frequency, mean burst duration, and mean duration between bursts.

Conclusion: The study showed that inductions of labor that took less than 24 h to deliver have a higher mean power in the baseline electrophysiological activity of the uterus when recorded prior to planned induction. The results are indicative that baseline electrophysiological activity measured prior to induction is associated with successful induction.

1. Introduction

Induction of labor has increased significantly across developed countries(Marconi, 2019), and especially in the United States and Europe where it is performed in approximately 1 in 3 deliveries (Zeitlin et al., 2013; Osterman et al., 2022). Additionally, induction of labor (IOL) has been assessed in many different facets over the years. Researchers have looked at several variables including nulliparous versus multiparous, medical versus mechanical, and single therapy versus dual therapy. Once induction is initiated, delivery may take up to 48–72 h; thus, obstetricians try to minimize the risk to patients and optimize resources on the labor and delivery unit when utilizing the procedure. Clinically, it is well known that, in many cases, the administration of oxytocin fails to induce effective labor contractions (failed induction), resulting in the need for a cesarean section (Lin and Rouse, 2006; Schoen and Navathe, 2015). The success of induction, or vaginal delivery within 24 h, relates to the electrophysiology of the uterus, since some patients respond to lower dosages of oxytocin while others need a higher dosage (Vasak et al., 2013, 2017). Excessive dosages of oxytocin can result in tetanic contractions, which can cause uterine rupture (Simpson and Knox, 2009; Al-Zirqi et al., 2017). The time of administration and dosage requirements, however, are not predictable based on current monitoring techniques including tocodynamometer (TOCO) and intrauterine pressure catheter (IUPC). In addition to measuring changes in cervical state,

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TOCO and IUPC monitor labor progression by measuring the rate, duration and amplitude of uterine contraction. Though widely used in clinical practice, TOCO is susceptibility to maternal motion artifacts. While, IUPC is more reliable and accurate than TOCO, it is invasive limiting its use to patients in whom delivery is necessary. With TOCO's poor predictive power and the invasive nature of IUPC, neither technique has been highly predictive in motoring progress of labor in general (Vlemminx et al., 2018).

Alternative methods to predict successful induction of labor are being assessed in an effort to reduce time spent in the labor and delivery unit at a busy tertiary-care referral center. These methods including transvaginal ultrasound (TVUS) assessment of the cervix, biochemical markers including fetal fibronectin (fFN) and insulin-like growth factor binding protein-1 (IGFBP-1) have been explored. None of these techniques have provided sufficient predictability to change clinical practice (Lazanakis et al., 2002; Dögl et al., 2011; Son and Miller, 2017). At the University of Arkansas for Medical Sciences (UAMS) we have a unique device, called SARA (SQUID Array for Reproductive Assessment), that can capture the uterine electrophysiology by non-invasive means over the maternal abdomen (Eswaran et al., 2002, 2004; Zhang et al., 2018). This device has 151 non-invasive sensors that can detect magnetic fields generated by electrical currents during tissue depolarization. The SARA's sensors, located just beneath its surface, are able to detect weak magnetic-field fluctuations emanating from deep within the human abdomen. The technique is referred to as magnetomyography (MMG), and is analogous to electromyography (EMG), although it has high spatial-temporal resolution and relatively low signal attenuation compared to the latter (Eswaran et al., 2002, 2004, 2009). Several uterine-activity parameters, including mean peak frequency, burst duration, and amplitude of contractions have been extracted from these MMG signals. These studies have also demonstrated a gradual increase in synchronized activity of the uterus close to onset of labor as well as an increase in relative strength of MMG activity in patients in active labor (Eswaran et al., 2004, 2009; Govindan et al., 2015).

The objective of this study was to record and characterize the uterine electrophysiological signals over the abdomen of pregnant women during the preparatory phase in patients scheduled for induction of labor at term in order to determine any association to a successful induction of labor.

2. Materials and methods

We conducted a prospective single-site observational study approved by the Institutional Review Board at UAMS. Inclusion criteria were women undergoing induction of labor at UAMS between 36 and 42 weeks gestational age in the cephalic position. Women were invited to participate in this study directly before planned induction of labor. Subject ID 23 was the only patient induced at 36 weeks gestational age. This patient had an earlier induction due to a twin pregnancy. After informed consent was obtained, participants were instructed to sit for 12 min while uterine electrophysiology signals were recorded with SARA. The method of induction of labor was based on the modified Bishop score, which includes only dilation, effacement and station, determined by the physician at the time of admission (Laughon et al., 2011). Methods for induction of labor included cervical ripening with prostaglandin E1 with addition of Foley bulb when feasible or combined Foley bulb and oxytocin. Participants either were placed on oxytocin initially or received an oxytocin drip once the cervix was favorable. Active labor was defined as a 6-cm dilation of the cervix. Cervical examinations were performed every 2 h to monitor labor. Active phase arrest was defined as no cervical change for $\geq$ 4 h despite adequate contractions, or no cervical change for $\geq$ 6 h with inadequate contractions, at which time a cesarean delivery was performed (Zhang et al., 2010a,b). All patients who underwent a cesarean section had an indication of failure to progress either due to active phase arrest of dilation or arrest of descent, however fetal intolerance of labor was an additional indication in a few study participants.

The MMG signals were collected at a sampling rate of 250 Hz and down sampled to 32 Hz. In the next step we applied a bandpass filter (0.1–1 Hz) to attenuate the interfering maternal and fetal cardiac signals. Further, a notch filter (0.25–0.35 Hz) was applied to suppress the maternal breathing which is a prominent signal around the frequency of 0.33 Hz. The contractile segments corresponding to uterine MMG burst activity present in each sensor was detected using an automated Wavelet and Hilbert transform approach as described previously in Furdea et al. (2009). The algorithm developed by our group uses a threshold that automatically identifies the true contractile events in the uterine biomagnetic data as described in Furdea et al., and successfully identifies bursts in the MMG signals per channel (Furdea et al., 2009). The subject-level uterine MMG parameters both in frequency and time domains were extracted. In the frequency domain, the mean spectral power and the mean peak frequency for the whole recording period (burst and quiescent) and for only the burst period were calculated across all sensors. In the time domain, the mean duration of burst, mean duration between bursts, and mean number of bursts was calculated from each burst activity detected across all sensors. The MMG data was correlated to additional information from the participant's labor record. The participant's modified Bishop's score at presentation, gravidity, parity, time to active labor, and maximum dosage and duration of oxytocin were recorded. The dosage of oxytocin and the success or failure of induction was tracked using patient clinical charts in labor and delivery. A spontaneous vaginal delivery within 24 h was classified as a successful induction of labor. Wilcoxon's rank-sum test with normal approximation was used to compare IOL successes to IOL failures for differences in gestational age (GA), parity, modified Bishop's score, maximum Oxytocin, and uterine MMG parameters. Results were summarized study-wide and by group using arithmetic averages and standard deviations (SDs). All tests employed an unadjusted $\alpha = 0.05$ significance level despite the multiple testing, in order not to inflate Type II (false-negative) error in this relatively small sample study.

3. Results

A total of 33 participants were enrolled in the study and two were excluded since MMG recordings were not completed due to technical issues. Table 1 provides participant characteristics from the 31 successful recordings including GA, Parity, presenting Cervical Dilation/Effacement/Station, Modified Bishop Score, time to active labor from initial oxytocin, maximum oxytocin (mU/min), Oxytocin Complete (mU/min) and mode of delivery. From the 31 successful MMG recordings obtained, 4 were excluded from analysis due to reasons explained in the flow chart shown in Fig. 1. Additionally, the flow chart in Fig. 1 details the number of participants that were included in the analysis and their distribution based on labor outcomes. Of the 27 subjects who contributed a data set, 19 (70%) had a spontaneous delivery within 24 h as opposed to 8 (30%) who exceeded 24 h. Eleven (41%) of the 27 subjects were nulliparous.

Based on the analysis of MMG signals displayed in Table 2, the average number of bursts among all study subjects was 1.9, and their average duration was 44.5 s. The mean power spectral density amplitude and frequency were 0.18 $fT{\cdot}Hz^{-1/2}$ and 0.44 Hz, respectively. Fewer than half (5/11) of the nulliparous subjects had a successful IOL, compared to 88% (14/16) of the multiparous subjects (Fisher's exact $p = 0.033$). When parity was analyzed as a continuous variable, Table 2 shows that average parity was three times higher among successful inductions (Average (SD) = 1.53 (1.47)) than among unsuccessful ones (0.50 (1.07)) ($p = 0.039$). Similarly, modified Bishop score was two times higher, on average, among IOL successes (3.32 (1.95)) than among IOL failures (1.63 (2.07)) ($p = 0.032$), whereas gestational age and maximum oxytocin showed non-significant differences between the two groups. With respect to MMG measures of uterine activity, successful IOLs showed sharply elevated mean power compared to failed IOLs, but

Table 1
Characteristics of 31 subjects with successful MMG recordings.

Subject ID	GA	Parity	Presenting Cervical Dilation/ Effacement/Station	Modified Bishop Score	Time to AL from Initial Oxytocin	Maximum Oxytocin received	Oxytocin at Complete	Delivery
1	39w0d	0	1cm/75%/-2	4	9h26m	18mU/min	18mU/min	SVD
3	39w0d	1	4cm/75%/-3	4	3h19m	10mU/min	10mU/min	SVD
4	37w0d	1	6cm/75%/-1	7	–	10mU/min	10mU/min	SVD
5	38w1d	1	4cm/70%/-2	5	7h45m	6mU/min	6mU/min	SVD
7	38w0d	1	2cm/25%/-2	2	11h45m	22mU/min	0mU/min	SVD
8	39w5d	0	.5cm/thick/-3	0	14h45m	22mU/min	22mU/min	SVD
9	38w6d	4	5cm/50%/-2	5	3h50m	6mU/min	none	SVD
10	40w0d	0	1cm/thick/high	1	19h39m	42mU/min	42mU/min	SVD
11	38w5d	2	2cm/25%/-2	2	5h25m	12mU/min	12mU/min	SVD
12	38w4d	1	fingertip/thick/high	0	31h45m	6mU/min	6mU/min	SVD
13	38w3d	0	1cm/50%/-2	3	3h5m	14mU/min	14mU/min	SVD
14	40w4d	1	1cm/thick/high	1	9h15m	8mU/min	8mU/min	SVD
15	40w6d	0	closed/thick/high	0	–	–	–	LTCS
16	40w1d	1	4–5cm/80%/-2	6	3h29m	12mU/min	12mU/min	SVD
17	39w4d	2	3cm/25%/-2	3	13h9m	20mU/min	20mU/min	SVD
18	38w4d	0	1cm/thick/high	1	20h	22mU/min	–	LTCS
19	38w0d	0	3cm/25%/-3	2	9h50m	12mU/min	12mU/min	SVD
20	39w2d	0	1cm/25%/-3	1	4h45m	36mU/min	–	LTCS
21	41w1d	0	5cm/50%/-1	6	–	12mU/min	12mU/min	LTCS
22	38w6d	0	closed/thick/high	0	15h47m	36mU/min	–	LTCS
23[a]	36w0d	3	5/75/-1	7	1h25m	6mU/min	6mU/min	SVD
24	40w6d	0	fingertip/thick/high	0	29h25m	20mU/min	–	LTCS
25	40w3d	1	2cm/50%/-2	3	8h42m	12mU/min	12mU/min	SVD
26	38w1d	3	2cm/50%/-2	3	13h30m	2mU/min	none	SVD
27	41w0d	2	4cm/50%/-2	4	5h36m	10mU/min	10mU/min	SVD
28	38w6d	3	2cm/50%/-2	3	16h28m	20mU/min	18mU/min	SVD
29	37w6d	0	2cm/50%/-3	2	6h4m	18mU/min	18mU/min	SVD
30	38w0d	1	4cm/50%/-2	4	6h6m	22mU/min	22mU/min	SVD
31	41w0d	0	1.5cm/50%/-3	2	19h30m	42mU/min	–	LTCS
33	41w0d	3	2cm/50%/-3	2	3h50m	12mU/min	12mU/min	SVD
34	40w1d	5	2cm/thick/high	1	9h44m	12mU/min	12mU/min	SVD

SVD: Spontaneous Vaginal Delivery; LTCS: Low transverse cesarean section.
[a] Subject ID 23 was the only patient induced at 36 weeks gestational age. This patient had an earlier induction due to a twin pregnancy.

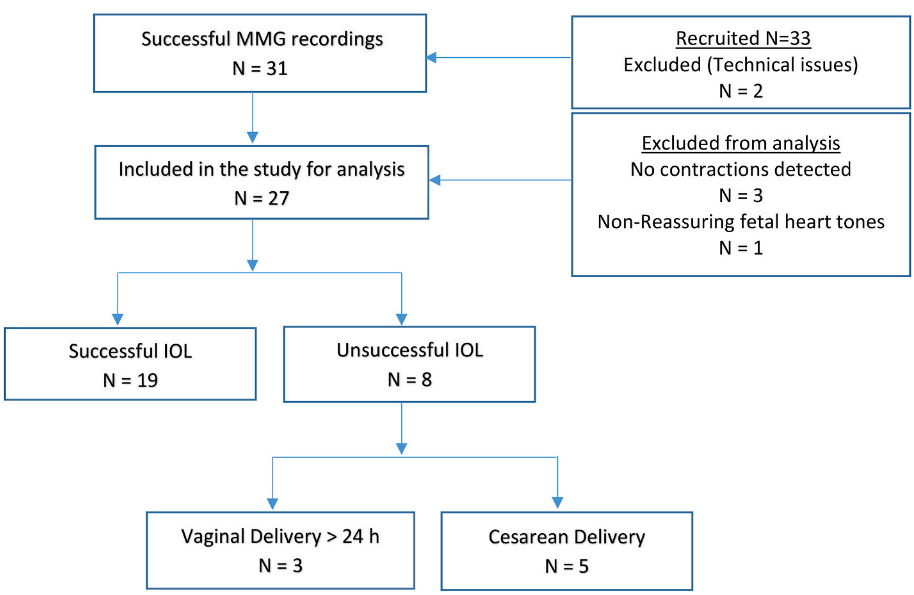

Fig. 1. Flow Diagram of included and excluded patients in the study.

slight differences (non-significant) in mean peak frequency, mean burst duration, or mean duration between bursts from Table 2. Specifically, average mean power among successful compared to failed IOLs was 3.5 times higher during burst activity (2.46 (0.456) versus 0.070 (0.074), respectively) ($p = 0.034$) and four times higher over the recording as a whole (0.235 (0.560) versus 0.054 (0.051), respectively) ($p = 0.038$). Finally, the mean number of bursts detected had an average (SD) of 2.05 (0.45) among IOL successes compared to 1.68 (0.24) among IOL failures ($p = 0.038$). Fig. 2 displays the distribution of mean power in the frequency band based on a successful induction of labor with spontaneous vaginal delivery within 24 h or not for during contractions and the whole recording.

4. Discussion

Magnetomyography provided an insight into the global

Table 2
Bishop Score and MMG Comparative Analysis (27 subjects) between success and failure of induction of labor.

Recorded Parameters	Entire Study (N = 27): Average (SD)[a] Median (Q1, Q3)[†]	IOL Success (N = 19): Average (SD)[a] Median (Q1, Q3)[†]	IOL Failure (N = 8): Average (SD)[a] Median (Q1, Q3)[†]	Wilcoxon rank-sum P-value
GA (weeks)	39.2 (1.34) 39.0 (38.1, 40.4)	39.0 (1.37) 39.0 (38.0, 40.1)	39.6 (1.25) 39.4 (38.6, 40.9)	0.312
Parity	1.22 (1.42) 1 (0, 2)	1.53 (1.47) 1 (0, 3)	0.50 (1.07) 0 (0, 0.5)	0.039*
Modified Bishop Score	2.81 (2.09) 3 (1, 4)	3.32 (1.95) 3 (2, 4)	1.63 (2.07) 1 (0, 2.5)	0.032*
Maximum oxytocin (mU/min)	16.6 (10.2) 12.0 (10.0, 22.0)	14.0 (5.4) 12.0 (10.0, 20.0)	22.8 (15.8) 21.0 (9.0, 39.0)	0.218
Mean Power – whole recording ($fT/\sqrt{Hz}$)	0.182 (0.474) 0.060 (0.026, 0.143)	0.235 (0.560) 0.060 (0.030, 0.180)	0.054 (0.051) 0.023 (0.019, 0.089)	0.038*
Mean Power – during burst activity ($fT/\sqrt{Hz}$)	0.194 (0.390) 0.063 (0.030, 0.219)	0.246 (0.456) 0.083 (0.038, 0.238)	0.070 (0.074) 0.030 (0.018, 0.120)	0.034*
Mean Peak Frequency – whole recording (Hz)	0.436 (0.052) 0.423 (0.399, 0.487)	0.441 (0.053) 0.425 (0.400, 0.493)	0.426 (0.052) 0.414 (0.387, 0.448)	0.507
Mean Peak Frequency – during burst activity (Hz)	0.452 (0.040) 0.455 (0.416, 0.480)	0.459 (0.039) 0.461 (0.432, 0.483)	0.436 (0.038) 0.416 (0.412, 0.456)	0.152
Mean Duration of Burst (sec)	44.5 (11.0) 42.0 (36.2, 50.6)	45.8 (11.4) 44.9 (37.3, 51.6)	41.3 (9.9) 39.3 (32.7, 49.2)	0.339
Mean Duration between Bursts (sec)	84.3 (60.9) 71.6 (55.5, 95.5)	91.4 (66.8) 87.7 (56.8, 99.5)	67.5 (42.6) 61.5 (42.1, 77.0)	0.202
Mean Number of Bursts detected across all sensors	1.94 (0.43) 1.86 (1.59, 2.14)	2.05 (0.45) 1.95 (1.69, 2.32)	1.68 (0.24) 1.62 (1.54, 1.82)	0.038*

[a] (SD): Standard Deviation. †(Q1, Q3): First and third quartiles. *statistically significant at $\alpha = 0.05$.

electrophysiological state of the uterine activity both during quiescent and active phases. This study showed that inductions of labor that took less than 24 h to deliver have a higher mean power in baseline electrophysiological activity of the uterus when recorded prior to planned induction. This was also reflected in the low-level uterine burst activity detected in the IOL failure group which is a result of global summation of action potentials. The higher mean power in power spectral distribution relates to potentially higher baseline synchrony in the electrical activity, as past studies tracking of uterine electrophysiological activity in term patients over a time period have shown a gradual increase in synchrony as the women gets close to labor (Eswaran et al., 2009; Govindan et al., 2015). Most of these electrophysiological studies have highlighted the fact that the uterus undergoes a preparatory phase before it is ready to proceed into labor. Our results in this study are indicative of the fact that baseline electrophysiological activity measured prior to induction could serve as a predictor of successful induction. Correspondingly, in terms of the clinical indicators, the modified Bishop Score was statistically significant between IOL success and failure groups. We propose that this observation is consistent with that fact that higher levels of uterine preparedness as observed by MMG prior to labor lead to stronger and effective contractions that allow for a more favorable cervix.

Our reported mean peak frequencies are similar to non-laboring patients reported in several uterine EMG results (Garfield et al., 2005; Garfield and Maner, 2007; Lucovnik et al., 2011; Vasak et al., 2017). The fact that the mean peak frequency of the burst, burst duration and inter-burst duration were not significant between the two groups was not surprising. Most of the recorded changes, especially in the mean peak frequency, occur only as labor progresses including when labor is augmented (Vasak et al., 2013). Additionally, in a follow up study by Vasak et al. (2017), they observed no correlation in mean peak frequency in induced labor with respect to progression of labor as they were tracked from the onset of labor or at first stage of labor until delivery.

It has been well documented that typically nulliparous women at term often fail to progress after being induced resulting in caesarian deliveries (Zhang et al., 2010a,b; Laughon et al., 2012; Vasak et al., 2013). As seen from our results, the mean parity in the IOL success group was significantly higher than the of failure group. The difference is evident even in the uterine electrical activity that was recorded over weeks prior to reaching active labor as reported by Govindan et al. (2015). In their study, the mean synchronization index, which is a measure of global electrical activation of the uterus, increased twice as fast in the non-nulliparous women compared to the nulliparous. MMG provides a more precise electrophysiological status of the uterus since this activity reflects the readiness of the uterus to go into labor. This insight may evolve to a be predictor compared to parity alone.

The major limitation of our study was its small sample size. Also the

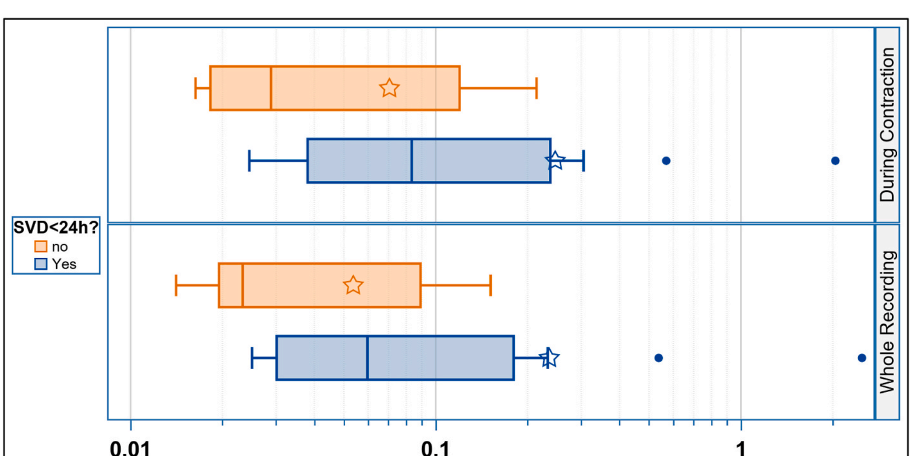

Fig. 2. Distributions by SVD Group of Mean Power During Contraction (*top*) and over the Whole Recording (*bottom*). The horizontal axis displays the Mean Power (units = $fT/\sqrt{Hz}$) of individual recordings. Boxes cover interquartile ranges while the vertical lines inside them mark medians. Stars denote group means. Filled circles and whiskers respectively represent outliers and non-outliers outside the interquartile ranges. Figure legend to the left displays if spontaneous vaginal delivery was within 24 h which determined induction of labor success.

relatively short recording time would have precluded us from observing contractile activity in the three of the excluded subjects. In future it will be worthwhile examining the quiescent period across longer recordings irrespective of the prescence or absence of contractions. Further due to the limited sample size, the presence of only eight subjects in the IOL failure group precluded us from conducting a multivariate logistic-regression analysis of IOL outcome using uterine MMG parameters as predictors while adjusting for parity and modified Bishop score. Our goal in this study was to quantify the electrophysiological status of the women prior to induction. Although Bishop score was recorded as a reference marker in this study, the purpose was not to evaluate the score itself for its effectiveness. We however acknowledge the success of IOL can be influenced by the intervention that is guided by the Bishop score including the dosage and the timing of prostaglandin E1 with addition of Foley bulb or combined Foley bulb and oxytocin.

On the other hand, there are only a few studies that have examined the electrophysiological aspects of the preparedness prior to labor both before and during the induction process (Benalcazar-Parra et al., 2018, 2019, 2019; Benalcazar-Parra et al., 2019a,b; Diaz-Martinez et al., 2023). Benalcazar-Parra et al. showed that in the case of prostaglandin E1 (Misoprostrol) administration, successful induction was related to increase in electrophysiological activity both terms of amplitude and frequency content of the bursts (Benalcazar-Parra et al., 2018). Our study using MMG are results comparative to these referenced studies as they also conclude that electrophysiological measures can potentially be used to predict successful labor induction. In a follow up study from the same group, uterine EMG was evaluated in a prediction model based on clinical obstetric observations, EMG parameters and the combination of the two. They concluded that uterine electrophysiological parameters can potentially be used to predict successful lOL since it outperforms the traditional obstetric features (Benalcazar-Parra et al., 2019a,b).

5. Conclusion

This study reveals that the electrophysiological activity of the uterus recorded by MMG provides an insight into the preparatory state of the uterus before a planned induction. We observed that successful inductions of labor, less than 24 h from induction to spontaneous vaginal delivery, were found to have higher mean power baseline electrophysiological activity of the uterus when recorded prior to induction. The significant difference for induction of labor success based on parity supports the idea that nulliparous women have a greater tendency to fail to progress after labor induction. Additionally, the significance of the Bishop score demonstrates the possibility that greater uterine preparedness prior to labor allows for a more favorable cervix. Our results are indicative that baseline electrophysiological activity especially as it relates to mean spectral power measured prior to induction has an association with successful induction.

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CRediT authorship contribution statement

Sarah T. Mehl: Formal analysis. **Pamela M. Simmons:** Conceptualization. **Julie R. Whittington:** Conceptualization. **Eric R. Siegel:** Formal analysis. **Curtis L. Lowery:** Conceptualization. **Lauren D. Crimmins-Pierce:** Formal analysis. **Hari Eswaran:** Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Hari Eswaran reports financial support was provided by National Institutes of Health.

Data availability

Data will be made available on request.

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