Dynamic Changes in the Myometrium during the Third Stage of Labor, Evaluated Using Two-Dimensional Ultrasound, in Women with Normal and Abnormal Third Stage of Labor and in Women with Obstetric Complications

Manasi Patwardhan^a Edgar Hernandez-Andrade^{a, b} Hyunyoung Ahn^{a, b}
Steven J. Korzeniewski^{a, b} Alyse Schwartz^b Sonia S. Hassan^{a, b} Roberto Romero^{b–d}

^aDepartment of Obstetrics and Gynecology, Division of Maternal Fetal Medicine, Wayne State University, Detroit, Mich., ^bPerinatology Research Branch, NICHD/NIH/DHHS, Bethesda, Md., Detroit, Mich., ^cDepartment of Obstetrics and Gynecology, University of Michigan, Ann Arbor, Mich., and ^dDepartment of Epidemiology and Biostatistics, Michigan State University, East Lansing, Mich., USA

Key Words

Pregnancy · Labor · Myometrial thickness · Uterine contractions · Postpartum hemorrhage · Clinical chorioamnionitis · Preterm delivery · Prolonged third stage of labor

Abstract

Objective: To investigate dynamic changes in myometrial thickness during the third stage of labor. **Methods:** Myometrial thickness was measured using ultrasound at one-minute time intervals during the third stage of labor in the mid-region of the upper and lower uterine segments in 151 patients including: women with a long third stage of labor (n = 30), postpartum hemorrhage (n = 4), preterm delivery (n = 7) and clinical chorioamnionitis (n = 4). Differences between myometrial thickness of the uterine segments and as a function of time were evaluated. **Results:** There was a significant linear increase in the mean myometrial thickness of the upper uterine segments, as well as a significant linear decrease in the mean myometrial thickness of the lower uterine seg-

ments until the expulsion of the placenta ($p < 0.001$). The ratio of the measurements of the upper to the lower uterine segments increased significantly as a function of time ($p < 0.0001$). In women with postpartum hemorrhage, preterm delivery, and clinical chorioamnionitis, an uncoordinated pattern among the uterine segments was observed. **Conclusion:** A well-coordinated activity between the upper and lower uterine segments is demonstrated in normal placental delivery. In some clinical conditions this pattern is not observed, increasing the time for placental delivery and the risk of postpartum hemorrhage.

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Introduction

Abnormalities of the third stage of labor such as prolonged duration and retained placenta can be associated with postpartum hemorrhage, which is one of the leading causes of maternal mortality [1–9]. Although risk factors for an abnormal third stage of labor [2, 3, 10–13] and in-

formation on the process of placental delivery have been reported [14–21], data on myometrial activity during a normal and an abnormal third stage of labor are still limited [22–26].

During pregnancy the uterus shows dynamic activity related to plasma concentrations of mediators that influence myometrial contractility, namely oxytocin and prostaglandins and their receptors [27–32]. The uterine contractions vary in intensity and characteristics during labor; the upper uterine segment exhibits a contractile nature, and the lower segment a relaxation process in order to facilitate the passage of the fetus [33–35]. Whether this functional disparity exists in the third stage of labor has not been explored. Variations in myometrial activity may contribute to, or could be associated with, complications of the third stage of labor. These variations might be related to the intensity and duration of contractions [22, 25, 36] or to different patterns of uterine contractility [37–39].

A noninvasive method to evaluate dynamic changes in the myometrium is ultrasound [40–42]. Ultrasound can provide a continuous assessment of changes in the thickness of the myometrium during a normal and an abnormal third stage of labor. In this study, we aimed to apply ultrasound to evaluate dynamic changes in myometrial thickness in different uterine segments as an indirect evaluation of uterine contractions in women with normal and prolonged third stage of labor, as well as in women with obstetric complications.

Methods

This observational study was performed on 151 women after vaginal delivery in the labor and delivery unit of Hutzel Women's Hospital, Detroit Medical Center, Detroit, Michigan, USA. All women provided written informed consent, which was approved by the Institutional Review Boards of Wayne State University, and the National Institute of Health/National Institute of Child Health and Human Development (NIH/NICHD). The inclusion criteria were women of gestational ages between 30 and 42 weeks of pregnancy who delivered by spontaneous or assisted vaginal delivery. Women with obstetric complications such as preterm delivery, clinical chorioamnionitis, prolonged third stage of labor, and postpartum hemorrhage were also included. The exclusion criteria were breech presentation, placenta previa, and women requiring a cesarean section. Active management of the third stage of labor (uterine massage, oxytocin, and controlled cord traction) and the use of other uterotonic agents were employed only if deemed medically necessary by the attending physician.

A 2–5 MHz curvilinear transducer (Voluson E8) was used for all of the examinations. Continuous visualization of the uterus was performed in a midsagittal view to obtain the upper and lower uterine segments in the same image; depth was adjusted to include

Fig. 1. Sonographic measurements of the myometrium during third stage of labor. AUS = Anterior upper segment; PUS = posterior upper segment; ALUS = anterior lower uterine segment; PLUS = posterior lower uterine segment.

only the uterus, and gain was adjusted to obtain a clear interphase between the uterus and the placenta. Ultrasound recordings were obtained from the moment of fetal delivery until the complete expulsion of the placenta. Maternal abdominal aorta was used as a reference point for maintaining consistency in obtaining the midsagittal plane of the uterus [43].

Myometrial measurements were performed offline at one-minute time intervals by one examiner who placed the calipers at the respective echogenic interfaces of the serosa and the decidua with the myometrium. The myometrium was defined as a sonographically echoic homogenous layer between the serosa and the decidua. Myometrial thickness was measured at four different sites in a plane perpendicular to that of the myometrium: (1) anterior upper uterine segment (AUS) at 2.0 to 3.0 cm on the anterior wall from the change in the curvature of the uterine fundus; (2) posterior upper uterine segment (PUS) at 2.0 to 3.0 cm on the posterior wall from the change in the curvature of the uterine fundus; (3) anterior lower uterine segment (ALUS) at the reflection of the maternal urinary bladder in the anterior wall of the uterus; and (4) posterior lower uterine segment (PLUS) directly inferior to the measurement of the ALUS (fig. 1).

The number of studied subjects was estimated in the following manner: assuming that the process of placental delivery is related to differences in the thickness between the upper uterine and lower uterine segments, we postulated that the upper segment should have at least double thickness compared to the lower uterine segment (100% difference) for a spontaneous placental delivery; therefore, with a Type I error probability (α) set at 5%, a sample size of at least 85 subjects would provide a power of 90%.

Statistical Analysis

Two datasets were created using the same myometrial measurements. The first dataset was obtained with delivery of the fetus as minute '0' to evaluate the myometrial changes in relation to the time of fetal delivery; the second dataset was obtained with the delivery of the placenta considered minute '0' to evaluate the myometrial changes in relation to the time of placental expulsion.

Table 1. Demographic and clinical characteristics of the study group (n = 151)

n = 151	Median or n	Range or percentage (*IQR)
Maternal age, years	24	15–41 (21–30)
Gestational age, weeks	39.4	31.3–42 (38.5–40.3)*
Term delivery	144	95.4%
Preterm delivery	7	4.6%
Primiparous	21	13.9%
Abortions (spontaneous/surgical/medical)	58	38.4%
Multiple pregnancy	1 (twin pregnancy)	0.7%
Body mass index (BMI), kg/m ²	30	16–63 (26–35)*
BMI ≥30, kg/m ²	87	57.6%
Placental location		
Anterior	80	53%
Posterior	65	43%
Estimated blood loss, ml	300	100–600 (250–350)*
Postpartum hemorrhage (≥500 ml, requiring uterotonics)	4	2.6%
Previous history of cesarean section	9	6%
Clinical chorioamnionitis	4	2.6%
Induction of labor	58	38.4%
Oxytocin use in labor	93	61.6%
Epidural in labor	133	88.1%
Oxytocin during third stage of labor	1	0.7%
Duration of second stage of labor, min	20	1–305 (9–51)*
Duration of third stage of labor, min	8	2–39 (6–12)*
Latent phase, s	163	92–249*
Detachment phase, s	100	40–203*
Expulsion phase, s	164	88–304*

* Expressed as interquartile range (IQR); BMI = Body mass index; s = seconds.

The data that were not normally distributed as determined by the Kolmogorov-Smirnov test were log² transformed to better meet parametric assumptions. Comparisons between the groups were performed using Fisher's exact, Chi-square, and Mann Whitney U tests. Linear mixed models were used to estimate differences in the mean measurements as a function of time. The data from women with obstetric complications were compared with that of normal cases. Intraobserver reliability was evaluated by Spearman's correlation coefficient to test for correlation between repeated measurements at the four uterine segments.

Results

There were 151 women who participated in this study, including: women with a long third stage of labor (n = 30), postpartum hemorrhage (n = 4), preterm delivery (n = 7) and clinical chorioamnionitis (n = 4). All patients with postpartum hemorrhage responded to uterotonics (oxytocin 10–20 units in 500 ml/30 min; none of them went back to the operating room for removal of retained prod-

ucts. There was excellent intraobserver reliability for repeated measurements at all four uterine segments (Spearman's rho: AUS 0.94; PUS 0.98; ALUS 0.97; PLUS 0.95).

Duration of the Third Stage of Labor

The median duration of the third stage of labor was eight minutes (range 2–39 min) (table 1). Duration of the third stage of labor was divided into quartiles; 80% of the women were located in the first three quartiles and delivered their placentas within 12 min. These three quartiles were considered as a normal duration of the third stage of labor. The uppermost quartile was more than 12 min and was considered a long third stage of labor. There were no demographic differences among women with a normal or with a long third stage of labor (table 2).

Dynamic Changes in Myometrial Measurements in the Third Stage of Labor

In all 151 women, the median myometrial measurements changed dynamically during the entire third stage

Table 2. Demographic and clinical characteristics of women with a normal or long third stage of labor

Patient characteristics	Normal third stage of labor (≤ 12 min) (n = 120) median or n (% , range)	Long third stage of labor (> 12 min) (n = 31) median or n (% , range)	p value*
Age, years	25 (21–30)	24 (22–28)	0.7
Gestational age at delivery, weeks	39.4 (38.3–40.3)	39.3 (39.1–40.2)	0.5
Body mass index, kg/m ²	30 (27–36)	31 (25–33)	0.2
Placental location			
Anterior	65 (55)	14 (52)	0.7
Posterior	53 (45)	13 (48)	0.7
Induction of labor	49 (41)	9 (29)	0.2
Oxytocin use in labor	72 (60)	20 (65)	0.6
History of abortions	46 (39)	12 (39)	0.9
Medical diseases	21 (18)	9 (29)	0.1
History of Cesarean section	8 (7)	1 (3)	0.7
Clinical chorioamnionitis	2 (2)	2 (6)	0.2
Multiparous	103 (87)	26 (84)	1.0
Multiple pregnancy	1 (1)	0 (0)	1.0
Postpartum hemorrhage	3 (3)	1 (3)	1.0
Term delivery	113 (94)	30 (97)	0.3
Preterm delivery	7 (6)	0 (0)	0.3
Pitocin given in 3rd stage of labor	1 (1)	0 (0)	1.0
Epidural	105 (88)	27 (87)	1.0

* Chi-square or Fischer's exact.

of labor. These dynamic changes followed a similar pattern in the anterior and posterior parts of the uterus (fig. 2a, b; table 3). The overall thickness of the upper uterine segments was higher and significantly different than that of the lower uterine segments, with the two segments demonstrating more pronounced differences closer to the delivery of the placenta.

Comparisons between Women with Normal and Long Third Stages of Labor

There was a significant difference in the median myometrial thickness of the upper and lower anterior uterine segments among women with normal or long duration of the third stage of labor (table 3). The mean myometrial measurements of the upper uterine segments in both groups increased significantly as a function of time ($p < 0.001$; fig. 3), but were higher in women with normal duration of the third stage during the first minutes after fetal delivery; however, the measurements equalized prior to placental delivery (fig. 3). The mean myometrial measurements of the lower uterine segments in both groups decreased significantly as a function of time ($p < 0.001$; fig. 4). The slope of decline of the mean myometrial measurements in the normal third stage group was steeper

compared with that of the long third stage group during the entire third stage. The ratio of measurements of the upper to lower anterior uterine segments, and the upper to lower posterior uterine segments leading up to the delivery of the placenta increased significantly as a function of time, and there was no difference between the two ratios in the normal third stage of labor group ($p < 0.0001$; fig. 5).

Pregnancies with Obstetric Complications

Overall, there were no differences in the median myometrial measurements of the uterine segments between women with and without postpartum hemorrhage, or between women with and without chorioamnionitis (table 3). There was a significant difference in the median myometrial measurements of the anterior upper uterine segments, and the lower uterine segments between the term and preterm delivery groups; the median myometrial measurements of the posterior lower uterine segments were different; however, these differences were not statistically significant (table 3). For most of the third stage duration, the postpartum hemorrhage group appeared to have a thinner lower uterine segment, the preterm delivery group appeared

Fig. 2. Dynamic changes in myometrial thickness in the third stage of labor in all women and in women with obstetric complications. Minute 1 corresponds to placental delivery. AUS = Anterior upper segment; PUS = posterior upper segment; ALUS = anterior lower uterine segment; PLUS = posterior lower uterine segment.

to have a less clearer distinction between the upper and lower uterine segment measurements, and the clinical chorioamnionitis group did not appear to demonstrate dynamic changes in the upper and lower uterine segment measurements as compared to their respective controls. In the time period immediately prior to placental expulsion, the upper segments in these women followed a distinctive pattern of increasing median myometrial thickness and the lower segments followed a pattern of decreasing median myometrial thickness (fig. 2a, b).

Discussion

Principal Findings: (1) there is a continuous increment in the thickness of the upper uterine segment and a continuous reduction in the thickness of the lower uterine segment over time during the third stage of labor leading to placental delivery; (2) the myometrium differs significantly in thickness and demonstrates a slower rate of changes in thickness in women with a longer duration of the third stage of labor; (3) women with preterm delivery, postpartum hemorrhage and clinical chorioamnionitis demon-

Table 3. Comparison of median myometrial thickness between uterine segments

Group characteristics	Median myometrial thickness, cm	
All women (n = 151)		
AUS vs. ALUS	3	0.7*
PUS vs. PLUS	3	1*
Duration of third stage	normal (n = 120)	long (n = 31)
AUS	3	2.5*
PUS	3	2.7*
ALUS	0.8	0.7*
PLUS	1	0.8
Postpartum hemorrhage	yes (n = 4)	no (n = 147)
AUS	3	3
PUS	3	3
ALUS	0.6	0.7
PLUS	0.8	1
Term vs. preterm delivery	term (n = 144)	preterm (n = 7)
AUS	3	2*
PUS	3	2.9
ALUS	0.7	1.2*
PLUS	0.9	1.5*
Clinical chorioamnionitis	yes (n = 4)	no (n = 147)
AUS	2.5	3
PUS	2.7	3
ALUS	0.7	0.7
PLUS	0.8	1.0

AUS = Anterior upper segment; PUS = posterior upper segment; ALUS = anterior lower uterine segment; PLUS = posterior lower uterine segment. * $p < 0.05$; Mann Whitney.

strate a different pattern of changes in myometrial thickness during the third stage of labor as compared with uncomplicated patients.

Functional Importance of the Dynamic Changes of Myometrial Thickness during the Third Stage of Labor

The dynamic changes observed in myometrial thickness between the upper and lower uterine segments during the third stage of labor might be necessary for the process of placental detachment and expulsion. These differences can be a representation of a contractile phenomenon in the upper segment [40–42], and a relaxatory process in the lower uterine segment [33] probably influenced by the existing hormonal milieu (local and serum concentration of estrogen, progesterone, oxytocin, prostaglandin, corticotropin), as well as the delicate balance in the receptors among uterine segments [27–30, 33, 44–47].

There is limited ultrasound evidence to confirm that the upper and lower segments of the myometrium function differently [48]. Our data suggest that as the uterus prepares for the third stage of labor, it does so by functionally separating the upper and lower segments. The upper segment maintains and increases its thickness, which can be a manifestation of uterine retraction previously described as a gradual and permanent shortening of the uterine muscle after delivery; retraction might be important to prevent postpartum hemorrhage [49, 50]. Differences in thickness between the uterine segments can also represent other patterns of uterine activity as peristalsis [37, 38, 51], which has been previously associated with placental detachment [52]. Uterine peristalsis has been described using ultrasound and MRI techniques in nonpregnant women [53–65] as inherent, subtle, and rhythmic movements in the endometrium and the innermost zone of the myometrium [54], which is hormonally stimulated [56, 57, 66, 67]. In women with endometriosis, uncoordinated and arrhythmic uterine contractions have been described as ‘hyperperistalsis or dysperistalsis’ [67, 68].

Clinical Significance of the Dynamic Changes of Myometrial Thickness during the Third Stage of Labor

Our study demonstrated different patterns of myometrial activity during the third stage of labor in women with obstetric complications. Women with postpartum hemorrhage, clinical chorioamnionitis or preterm delivery showed similar averaged myometrial measurements as compared with uncomplicated patients; however, the pattern of myometrial thickness was distinctly different with a lack of coordinated changes in the upper and lower segments for most of the third stage duration. The highest odds for postpartum hemorrhage have been reported to be associated with risk factors such as chorioamnionitis and preterm delivery [2, 12, 13]; since the presence of these factors could potentially affect myometrial contractility [31, 69–72], the uncoordinated myometrial activity pattern observed in these women might be a contributing factor to their increased risk of postpartum hemorrhage. It could be speculated that this lack of coordination or dysperistalsis in myometrial activity seen in the third stage might be responsible for complications such as a prolonged third stage, and postpartum hemorrhage. However, even with diverse patterns in myometrial thickness, the final step was a gradual thickening of the upper uterine segment and thinning of the lower uterine segment, leading to spontaneous placental delivery.

Fig. 3. Dynamic changes in myometrium measurements in women with a normal (≤ 12 min) or long (> 12 min) third stage of labor of the upper uterine segments during the first 12 min after fetal delivery (a) anterior, (b) posterior, and during the last 12 min before placental delivery (c) anterior, (d) posterior.

Strengths and Weaknesses

The strengths of our study included a novel approach for the evaluation of myometrial thickness during the third stage of labor along with simultaneous assessment of the upper and lower uterine segments, and evaluation of different patterns of myometrial activity using real-time ultrasonography. Ultrasound has the advantage of providing a noninvasive and continuous visualization of the uterus as compared with other techniques previously used for evaluating the third stage of labor as intrauterine pressure catheter [26, 73–76], tocodynamometry [77] and electrical uterine myography [78].

The majority of women in our study underwent a natural third stage of labor without the use of active management (use of cord traction or uterotonics). Although our study consisted of a large sample size of low-risk pregnancies, it did not include pregnancies with retained placenta requiring manual removal. The number of women with

obstetric complications in our study was small, thus limiting the statistical analysis. Ultrasonographic evaluation in the third stage is unable to measure the contractile force of the uterine musculature as done by other techniques [22, 23]; therefore, a change in uterine thickness was used as a proxy for contractility. The quality of images obtained by ultrasound is subject to operator skills, body habitus of the subject, shadowing, and movement artifacts.

Conclusion

We demonstrated that the myometrium exhibits functional regionality by showing a contractile behavior in the upper segment and a relaxatory behavior in the lower segment during the third stage of labor. A well-coordinated activity between the upper and lower uterine segments is

Fig. 4. Dynamic changes in myometrium measurements in women with a normal (≤ 12 min) and long (> 12 min) third stage of labor of the lower uterine segments during the first 12 min after fetal delivery (a) anterior, (b) posterior, and during the last 12 min before placental delivery (c) anterior, (d) posterior.

Fig. 5. Dynamic changes in ratios of measurements between the anterior upper segment/anterior lower segment, and the posterior upper segment/posterior lower segment, in the third stage of labor. AUS = Anterior upper segment; PUS = posterior upper segment; ALUS = anterior lower uterine segment; PLUS = posterior lower uterine segment.

likely necessary for normal placental delivery. In some clinical conditions, this coordination is not achieved, increasing the time for placental delivery. In women with obstetric complications, it might be important to focus on the pattern of myometrial contractility, to reduce their risk of postpartum hemorrhage. Future studies focusing on the relationship between abnormal myometrial contractility and differences at a molecular level in the uterine segments might provide useful information for reducing third stage complications. The role of intrapartum sonography during labor, and the identification of risk factors related to postpartum hemorrhage have evolved over the years [79–123]. As we obtain more insight into the behav-

ior of the myometrium by ultrasound imaging, sonography [124] can become a useful noninvasive tool for assessing the third stage of labor.

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