OBSTETRICS

First stage of labor progression in women with large-for-gestational age infants

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BACKGROUND: Women with suspected large-for-gestational age fetuses have higher rates of dysfunctional labor and labor arrest diagnoses and, consequently, higher rates of cesarean deliveries. The identification of the factors that significantly affect labor progression of women with large-for-gestational age infants may better inform expected duration of labor for certain subgroups of this population.

OBJECTIVE: Because the standards for the first stage of labor when large-for-gestational age is present have not been defined clearly, the present study aims to evaluate labor progress of women with large-for-gestational age infants who complete the first stage of labor after 3-cm cervical dilation.

STUDY DESIGN: We conducted a retrospective cohort study of patients who were admitted for labor from 2004—2014 with a term vertex singleton who achieved 10-cm cervical dilation. Labor curves were constructed with repeated measures regression and were compared between patients who delivered large-for-gestational age infants (actual birthweight, >90th percentile for gestational age) and those who delivered appropriate-for-gestational age infants (actual birthweight, 10—90th percentile for gestational age). Interval-censored regression estimated median duration of labor after 3-cm cervical dilation stratified by actual infant birthweight and further stratified by parity (nulliparity vs multiparity), labor onset (spontaneous [augmented and not augmented] and induced labor), pregestational diabetes mellitus or gestational diabetes mellitus status, and maternal body mass index (obese, $\geq$30 kg/m^2 vs not obese, <30 kg/m^2). Multivariate analysis adjusted for confounding factors that were identified by bivariate analysis.

RESULTS: Among all 17,097 women who were included, 15,843 women (92.7%) had appropriate-for-gestational age infants; 1254 women (7.3%) had large-for-gestational age infants, of whom 387 (30.9%) were nulliparous; 464 women (37.0%) underwent induction of labor; 863 women (68.8%) were obese, and 158 women (12.6%) had diabetes mellitus or gestational diabetes mellitus. Women with large-for-gestational age infants had a slower progression from 3- to 10-cm cervical dilation compared with those with appropriate-for-gestational age infants (median, 8.57 hours [5th, 95th percentile, 2.95, 24.86] vs 6.46 hours [5th, 95th percentile, 2.23, 18.74]; $P<.01$). In the large-for-gestational age group, dilation from 6—10 cm progressed slower in nulliparous compared with multiparous women (3.28 hours [5th, 95th percentile, 0.71, 15.16] vs 2.03 hours [5th, 95th percentile, 0.44, 9.39]; $P<.01$) and in obese compared with not obese women (2.36 hours [5th, 95th percentile, 0.51, 10.91] vs 1.79 hours [5th, 95th percentile, 0.39, 8.31]; $P<.01$). Labor curves did not differ between large-for-gestational age and appropriate-for-gestational age groups when stratified by labor onset (nonaugmented spontaneous labor vs induced labor) or the presence of diabetes mellitus or gestational diabetes mellitus.

CONCLUSION: After 3-cm cervical dilation, the time required to reach the second stage of labor is greater in women with large-for-gestational age infants compared with those with appropriate-for-gestational age infants; these differences are most pronounced in nulliparous and obese women with large-for-gestational age infants in the active phase of labor (6—10 cm). Among women with large-for-gestational age infants, labor onset and presence of diabetes mellitus or gestational diabetes mellitus have no apparent effect on the duration of the first stage of labor after 3-cm cervical dilation.

Key words: diabetes mellitus, labor curve, labor onset, obesity, parity

Large-for-gestational age (LGA) describes an infant with birthweight >90th percentile for gestational age. The multiple factors that independently predispose women to having an LGA infant include preexisting maternal diabetes mellitus (DM), uncontrolled gestational DM (GDM), maternal prepregnancy obesity, and excessive gestational weight gain.[1–3] Aside from maternal obesity and DM status, the risk of having an LGA infant rises with increasing parity.[3]

Women with suspected LGA fetuses have higher rates of dysfunctional labor and labor arrest diagnoses and, consequently, higher rates of cesarean deliveries.[4,5] One group previously reported that labor arrest disorders and fetal macrosomia were responsible for 18% and 10%, respectively, of the overall increase in cesarean delivery rates that were observed over a 7-year study period.[6] Although LGA is not itself an indication for labor induction, US women with suspected LGA are more likely to undergo medically induced labor.[7] Moreover, induction of labor among women who carry LGA infants has been shown in some studies to be an independent risk factor for cesarean delivery.[8–12] Despite rising rates of cesarean deliveries performed in recent years, a concomitant decrease in maternal or neonatal morbidity or mortality rates has not been seen.[13,14]

Multiple factors that include parity, type of labor onset (induced vs spontaneous), maternal obesity, efficiency of uterine contractions, uterine infection, maternal pelvic dimensions, and fetal position are known to influence normal and abnormal labor progression.[15–21] However, the extent to which fetal size affects labor progression in

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AJOG at a Glance

Why was this study conducted?

Women with large-for-gestational age infants have higher rates of labor dystocia and arrest diagnoses than those with appropriate-for-gestational age infants. This study was conducted to evaluate the effect of infant birthweight and varying maternal characteristics on labor progression in women with large-for-gestational age infants.

Key findings

The overall duration of labor is significantly longer among women with large-for-gestational age infants compared with women with appropriate-for-gestational age infants, particularly in nulliparous and obese women in the active phase of labor (6−10 cm).

What does this add to what is known?

Our results provide an update to Friedman's early work and demonstrates significant prolongations in the active phase of labor among women who deliver infants with increased birthweight in the contemporary era in which labor has been shown to progress more gradually than initially reported.

contemporary populations remains unclear.[16] Identification of factors that significantly affect labor progression of women with LGA infants may better inform expected duration of labor for certain subgroups of this population. The present study aims to evaluate normal labor progression after 3-cm cervical dilation among women with LGA infants and maternal factors that modify labor progression specific to this population.

Materials and Methods

This was a retrospective cohort study from 2004−2014 of all consecutive women who were admitted for labor at term at a single, academic teaching hospital at Washington University in St. Louis, MO, who completed the first stage of labor. The study was approved by the Washington University School of Medicine Human Research Protection Office.

Eligible women for this cohort included women who presented either in spontaneous labor or for labor induction at term with a singleton pregnancy in cephalic presentation confirmed on ultrasound imaging on admission to labor and delivery. Exclusion criteria included women who delivered preterm, had fetuses with known congenital anomalies, or had placenta previa or other contraindication to vaginal delivery. For this analysis, we included only women who achieved 10-cm cervical dilation and excluded women who had small-for-gestational infants, which was defined by actual infant birthweight <10th percentile for gestational age.

Trained obstetric research personnel extracted detailed maternal sociodemographic information; medical, surgical and gynecologic history; and obstetric prenatal history, antepartum history and intrapartum course. Gestational age at delivery, parity, maternal comorbidities, labor onset, cervical examination times, dilation and station (measured on a −3 to +3 scale), length of labor stages, regional anesthesia, and mode of delivery were determined from documentation in the labor and delivery records. Term gestation was defined as ≥37 weeks 0 days of gestation that was determined by a women's last menstrual period and/or ultrasonographic dating. Cervical dilation was measured in centimeters from 0−10. The attending physician determined management plans for both spontaneous and induced labor. Providers at our institution consistently practice active labor management with cervical examinations at regular intervals every 2 hours primarily by resident physicians, with the use of early artificial rupture of membranes at cervical dilation of 3-4 cm with adequate head engagement, and with labor augmentation with oxytocin if no additional cervical dilation is made after 2 hours for all laboring patients. Actual infant birthweight that was obtained from the official pediatric delivery documentation was measured in grams approximately 1 hour after birth measured. Appropriate-for-gestational age (AGA) was defined as birthweight between the 10th and 90th percentile for gestational age, and LGA was defined as birthweight >90th percentile for gestational age as defined by the World Health Organization Child Growth Standards. Additionally, birthweight percentile cutoffs were determined according to the reference curve established by Duryea et al.[22]

Baseline characteristics of the study sample of women were tabulated and compared among women with AGA and LGA infants, with AGA used as the reference group. Categoric variables were examined with the use of the chi-squared or Fisher exact test. Continuous variables were compared with 1-way analysis of variance tests.

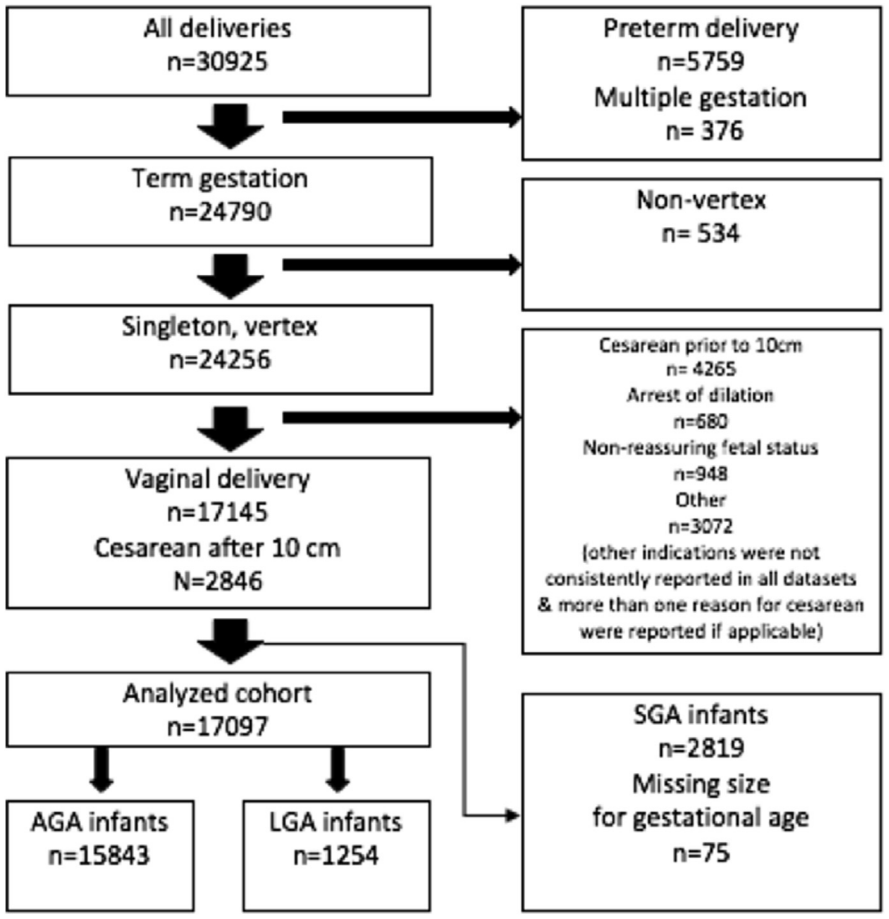
The primary outcome was median time of cervical dilation from 3−10 cm by 1-cm increments (eg, 3-4 cm), stratified by infant birthweight. Median time of cervical dilation from 6−10 cm, which defines the active phase of labor, was a secondary outcome. Interval-censored regression estimated median duration of labor, centimeter by centimeter, and were compared among women with AGA and LGA infants. The specific time of each 1-cm advancement in cervical dilation is not known precisely because cervical dilation is measured not continuously but rather over discrete intervals when a cervical examination occurs. The time interval from 1 cervical examination to the next for individual patients was fit to a log-normal distribution. The median 5th and 95th percentiles for labor duration at each interval of dilation was then estimated.[23,24] Confounding factors identified by bivariate analysis were adjusted for by multivariate analysis. Only those variables that were statistically significant ($P<.05$) were used in the final

model for the primary analysis that included maternal race, obesity (body mass index [BMI], ≥30 kg/m^2), DM, parity, labor onset, Bishop score ≥5 at admission, and previous cesarean delivery.

Average labor curves were constructed with the use of a repeated measures regression with a ninth-order polynomial model, which was determined to be the best fit for dilation values in our data, to compare labor progress according to actual infant birthweight in women with LGA vs AGA infants.[25] Use of a repeated-measures analysis reflects correlated cervical examinations in the same woman. The starting point for each labor curve was set at the time that a patient reached 10-cm cervical dilation because all patients in this cohort completed the first stage of labor. The regression analysis was performed in a reverse stepwise approach, with time to reach a given cervical dilation calculated backwards from 10−0 cm. This backward construction was performed because women arrived at the hospital typically after cervical dilation had occurred, and the exact timing of cervical progression before arrival to labor and delivery was unknown. The curves were then reversed after construction, with time to a given cervical dilation increasing from left-to-right along the x-axis consistent with traditional representation of time progression.

Labor curve construction and comparisons of median duration of labor among women with LGA infants were further stratified by parity (nulliparity vs multiparity), labor onset (spontaneous vs induced labor), presence or absence of maternal DM and/or GDM (DM/GDM), and obesity (nonobese defined as BMI, <30 kg/m^2, vs obese BMI, ≥30 kg/m^2, as measured on admission). Additional labor curves were constructed to evaluate whether there was an additive effect of having DM/GDM and obesity, having DM/GDM but not being obese, having neither DM/GDM nor obesity, and being obese but not having DM/GDM on labor progression in women with LGA infants. A test of interaction was performed to determine whether DM significantly interacted with the effect of obesity on labor progression among women with LGA infants. All statistical analysis was performed with Stata software (version 14; StataCorp, College Station, TX) and PROC LIFEREG of SAS software (version 9.4; SAS Institute Inc, Cary, NC). An alpha level <.05 was used to determine statistical significance.

FIGURE 1
Patient selection diagram



Flow chart of patient selection based on study exclusion and inclusion criteria.
AGA, appropriate-for-gestational age; *LGA*, large-for-gestational age; *SGA*, small-for-gestational age.
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Results

Among all 30,925 women who delivered at our institution during the study period (Figure 1), 17,097 women met inclusion criteria and were included in statistical analysis; 15,843 women (92.7%) had AGA infants, and 1254 women (7.3%) had LGA infants. Sixteen percent of the women, both among the AGA and LGA group, were excluded before achieving 10-cm cervical dilation for arrest of dilation. Of the 4265 women (13.8%) who delivered via cesarean section before achieving 10-cm cervical dilation during the study time period, 11.2% had LGA infants (n=476). Additionally, 9% of all women who delivered during the study period underwent cesarean section after 10 cm (n=2846), of whom 346 women (12.1%) had LGA infants.

Baseline characteristics for included women are given in Table 1; probability values were determined by nonparametric tests of the medians. Among the

TABLE 1
Baseline patient characteristics

Characteristic	Appropriate-for-gestational infants (n=15,843)	Large-for-gestational age infants (n=1254)	*P* value
Gestational age at delivery, wk[a]	39 (38–40)	39 (38–40)	<.01
Maternal age, y[b]	24.8±6.0	26.9±6.2	<.01
Black race, n (%)	10,474 (66.1)	604 (48.2)	<.01
Body mass index, kg/m^2[b]	31.8±7.3	34.7±7.8	<.01
Obesity (body mass index, ≥30 kg/m^2)[b]	8,237±52.0	863±68.8	<.01
Gravidity[a]	2 (1, 4)	3 (2, 4)	<.01
Parity, n (%)			<.01
Nulliparous	6,194 (39.1)	387 (30.9)	
Multiparous	9,649 (60.9)	867 (69.1)	
Mean birthweight, g[b]	3,299.6±329.5	4170.7±265.4	<.01
Bishop score on admission[a]	4 (2–6)	4 (2–6)	<.01
Initial dilation on presentation[a]	3 (2–5)	3 (2–5)	.6
Initial effacement on presentation[ac]	1.0 (0.5–2.0)	1.5 (0.5–2.0)	<.01
Initial station on presentation[ac]	−3 (−3 to −1)	−3 (−3 to −2)	<.01
Bishop score ≥5 at admission, n (%)	7,520 (47.5)	530 (42.3)	<.01
Labor onset, n (%)			.02
Spontaneous labor	10,492 (66.2)	790 (63.0)	
Induction of labor	5,351 (33.8)	464 (37.0)	
Mode of delivery, n (%)			<.01
Vaginal, spontaneous	12,582 (79.4)	839 (66.9)	
Vaginal, operative	1,152 (7.3)	69 (5.5)	
Cesarean section	2,109 (13.3)	346 (27.6)	
Epidural, n (%)	13,233 (85.5)	1044 (83.3)	.8
Previous cesarean delivery, n (%)	1,443 (9.1)	165 (13.2)	<.01
Hypertension of pregnancy, n (%)	1,508 (9.5)	129 (10.3)	.4
Diabetes mellitus, n (%)			
Gestational	432 (2.7)	97 (7.7)	<.01
Pregestational	156 (1.0)	61 (4.9)	<.01
Tobacco use, n (%)	2,270 (14.3)	123 (9.8)	<.01
Alcohol use, n (%)	195 (1.2)	5 (0.4)	.01
Illicit drug use, n (%)	1,503 (9.5)	67 (5.3)	<.01
Time of first stage of labor after 3-cm cervical dilation, min[a]	280.5 (140.8–499.8)	328.4 (172.4–542.6)	<.01
Time of second stage of labor, min[a]	27.5 (12.2–64.3)	38.8 (17.3–104.0)	<.01
Reason for second stage cesarean delivery, if necessary, n (%)[d]			
Nonreassuring fetal status	110 (0.7)	12 (1.0)	.29
Arrest of descent	222 (1.4)	41 (3.3)	<.01
Other	1833 (11.6)	301 (24.0)	<.01

[a] Data are given as median (interquartile range); [b] Data are given as mean±standard deviation; [c] Station was measured on a −3 to +3 scale; effacement was measured on a 0–3 scale, with 0 as fully 100% effaced and 3 as not at all effaced; [d] Indications for cesarean delivery were not mutually exclusive; multiple indications for cesarean delivery were reported in certain cases.

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women who achieved 10-cm cervical dilation with an AGA infant, 6194 (39.1%) were nulliparous, and 5351 (33.8%) underwent induction of labor. Among women who achieved 10-cm cervical dilation with an LGA infant, 387 (30.9%) were nulliparous, and 464 (37.0%) underwent induction of labor. DM/GDM was more common among women with LGA infants than those with AGA infants (12.6% vs 3.7%; $P<.01$). The patient population at our institution is 1 of particularly high morbidity with a significant minority underserved population. In our data set, we report high rates of obesity and a large black population. Obesity rates were higher among women who had LGA infants compared with those who had AGA infants (68.8% vs 52.0%; $P<.01$). Women who delivered LGA infants tended to be older and of higher parity. They were also more likely not to be black (51.8% vs 33.9%; $P<.01$), spend longer in both the first and second stages of labor, and have a higher likelihood of undergoing cesarean after 10-cm dilation with higher rates of arrest of descent. In fact, twice as many women with LGA infants underwent second stage cesarean delivery than did women with AGA infants (28.2% vs 13.7%; $P<.01$).

There was no difference in initial dilation on presentation ($P=.6$), use of regional anesthesia ($P=.8$), rates of hypertensive disorders of pregnancy ($P=.4$), or nonreassuring fetal status as the indication for second stage cesarean section between the LGA and AGA groups ($P=.3$). Among the women who were included, 37% in both groups presented before 3-cm cervical dilation (AGA, 5904 women; LGA, 459 women), whereas 63% in each group (AGA, 9939 women; LGA, 795 women) presented with cervical dilation ≥3 cm. Among women who presented in spontaneous labor, 31.2% and 22.3% of women in the AGA and LGA groups, respectively, received oxytocin augmentation. Among women who underwent labor induction, 89.7% and 80.9% of women in the AGA and LGA groups, respectively, received oxytocin as part of their induction.

TABLE 2
Time to reach a given cervical dilation after 3 cm

Cervical dilation (cm)	Appropriate-for-gestational age (n=15,843), hr	Large-for-gestational age (n=1254), hr	*P* value[a]
3–10	6.5 (2.2, 18.7)	8.6 (3.0, 24.9)	<.01
6–10	1.5 (0.3, 7.9)	2.2 (0.4, 11.8)	<.01
3–4	0.9 (0.1, 6.0)	1.3 (0.2, 8.3)	<.01
4–5	1.0 (0.2, 6.1)	1.4 (0.2, 9.2)	<.01
5–6	0.6 (0.07, 4.6)	0.8 (0.09, 6.2)	<.01
6–7	0.3 (0.04, 2.9)	0.5 (0.05, 3.8)	<.01
7–8	0.2 (0.03, 1.8)	0.3 (0.04, 2.4)	<.01
8–9	0.2 (0.03, 1.2)	0.3 (0.04, 1.9)	<.01
9–10	0.2 (0.02, 1.2)	0.2 (0.03, 1.7)	<.01

Note: Data are given as median hours (5th, 95th percentiles of the distribution).

[a] Adjustment made for race, obesity (body mass index, ≥30 kg/m^2), diabetes mellitus, parity, labor onset, Bishop score ≥5 at admission, and previous cesarean delivery.

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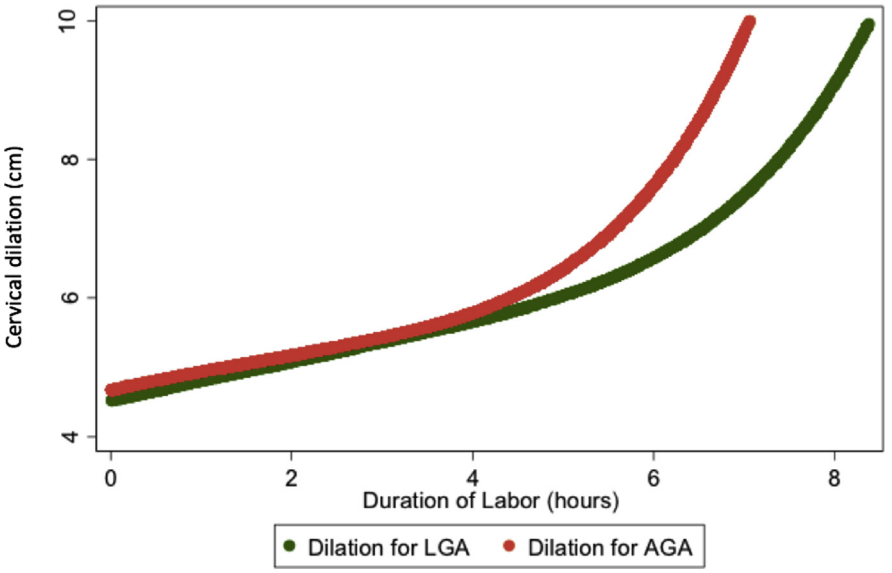
The median time to progress from 3–10 cm was longer in the LGA group (8.6 hours; 5th, 95th percentile, 3.0, 24.9; $P<.01$) than the AGA group (6.5 hours; 5th, 95th percentile, 2.2, 18.7; Table 2; Figure 2). The median time in hours in active labor (6–10 cm) was longer in the LGA group than in the AGA group by a median 0.7 hours ($P<.01$). The LGA group required a longer time to achieve each 1-cm increment of cervical dilation at all intervals from 3–10 cm, compared with the AGA group ($P<.01$).

FIGURE 2
Labor curves by size for gestational age, based on actual infant birthweight



Labor curves for time to progress from 0–10 cm cervical dilation in women with appropriate-for-gestational age and large-for-gestational age infants were based on actual infant birthweight.

AGA, appropriate-for-gestational age; *LGA*, large-for-gestational age.

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TABLE 3
Time to achieve 10 cm cervical dilation after 3 cm and 6 cm in women with large-for-gestational age infants according to parity, labor onset, diabetes mellitus/gestational diabetes mellitus, and obesity status

Variable	Cervical dilation, cm[a]	
	3–10	6–10
Parity		
Nulliparity (n=387)	11.2 (4.2, 29.9)	3.3 (0.7, 15.2)
Multiparity (n=867)	7.3 (2.7, 19.6)	2.0 (0.4, 9.4)
P value[b]	<.01	<.01
Labor onset		
Spontaneous labor, non-augmented (n=423)	4.2 (1.6, 11.1)	2.3 (0.5, 10.5)
Spontaneous labor, augmented with oxytocin (n=367)	7.6 (2.9, 20.5) *P*=.2[c]	2.6 (0.6, 11.9) *P*=.01[c]
Labor induction (n=464)	10.5 (3.9, 28.2) *P*=.06[c]	2.1 (0.5, 9.6) *P*=.6[c]
Diabetes mellitus/gestational diabetes mellitus status		
Yes (n=158)	8.4 (3.1, 22.5)	2.5 (0.5, 11.5)
No (n=1096)	7.4 (2.7, 19.7)	2.2 (0.5, 10.2)
P value[d]	.4	.3
Obesity status		
Body mass index, <30 kg/m^2 (n=391)	5.4 (2.0, 14.4)	1.8 (0.4, 8.3)
Body mass index, ≥30 kg/m^2 (n=863)	9.1 (3.4, 24.4)	2.4 (0.5, 10.9)
P value[e]	.2	.01

[a] Data given as median hours (5th, 95th percentiles of the distribution); [b] Adjustment for race, obesity (body mass index, ≥30 kg/m^2), diabetes mellitus, labor onset, Bishop score ≥5 at admission, previous cesarean. No missing data according to parity; [c] Adjustment for race, obesity (body mass index, ≥30 kg/m^2), diabetes mellitus, parity, Bishop score ≥5 at admission, previous cesarean delivery; no missing data according to labor onset; reference group for the probability values is the nonaugmented spontaneous labor onset group; [d] Adjustment for race, obesity (body mass index, ≥30 kg/m^2), parity, labor onset, Bishop score ≥5 at admission, previous cesarean delivery; the presence of diabetes mellitus/gestational diabetes mellitus was obtained from a written text field in the study database in which diabetes mellitus was listed for 158 patients along with other pregnancy complications; for all remaining patients, diabetes mellitus/gestational diabetes mellitus was not listed as a pregnancy complication in the database text field; [e] Adjustment for race, diabetes mellitus, parity, labor onset, Bishop score ≥5 at admission, previous cesarean delivery; patients with missing body mass index data were counted as not obese.

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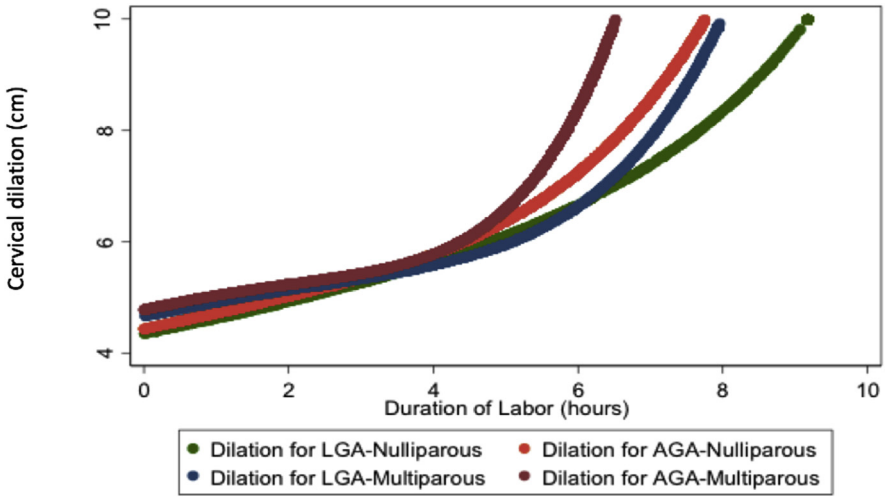
Among women with LGA infants, when stratified by parity (Table 3; Figures 3 and 4), the overall median time to progress from 3–10 cm and from 6–10 cm was significantly shorter among multiparous women compared with nulliparous women by a median 3.9 hours (*P*<.01) and 1.3 hours (*P*<.01), respectively. With regard to labor onset among women who delivered LGA infants (Table 3; Figure 5), the spontaneously laboring, nonaugmented women progressed 3–10 cm a median of 6.4 hours faster than did women who underwent labor induction, but this difference was not statistically significant (*P*=.06). No significant difference in time to dilate 6–10 cm (*P*=.6) was detected among spontaneously laboring, nonaugmented women compared with women who underwent labor induction. However, women with LGA infants who presented with spontaneous labor onset and were augmented with oxytocin (after not making cervical change on their own after 2 hours) experienced significantly slower labor duration in the active phase from 6–10 cm by a median of 0.7 hours (*P*=.01) compared with women with spontaneous labor onset who did not require oxytocin augmentation.

No significant difference in time to dilate 3–10 cm (*P*=.4) or 6–10 cm (*P*=.3) was identified among women who had DM/GDM with LGA infants compared with those women without DM/GDM (Table 3; Figure 6). Similarly, no significant difference in time to dilate 3–10 cm was identified among obese and not obese women with LGA infants (*P*=.2). However, obese women with LGA infants progressed from 6–10 cm a median of 0.6 hours (*P*=.01) more slowly compared with their not obese counterparts (Table 3; Figure 7).

Table 4 and Figure 8 demonstrate the combined effect of obesity and DM/GDM on labor progression. Compared with nonobese, nondiabetic women who delivered LGA infants, obese nondiabetic women progressed more slowly from 6–10 cm by a median of 0.6 hours (*P*=.01). However, diabetic women with LGA infants had similar rates of progression from 6–10 cm as did nondiabetic, nonobese women (*P*=.07), irrespective of obesity status. Obese women with DM/GDM had similar labor progression from 3–10 cm (median, 9.9 hours; 5th, 95th percentiles of the distribution, 3.7, 26.1; *P*=.6) and 6–10 cm (median, 2.2 hours; 5th, 95th percentiles of the distribution, 0.5, 10.6; *P*=1.0) compared with obese women without DM/GDM (3–10 cm: median, 8.98 hours; 5th, 95th percentiles of the distribution, 3.4, 23.8; 6–10 cm: median, 2.2 hours; 5th, 95th percentiles of the distribution, 0.5, 10.5). Diabetic women with obesity had similar labor progression from 3–10 cm (median, 9.1 hours; 5th, 95th percentiles of the distribution, 3.5, 23.5; *P*=.67) and 6–10 cm (median, 2.4 hours; 5th, 95th percentiles of the distribution, 0.5, 11.8; *P*=.4) compared with diabetic women with normal weight (BMI, <30 kg/m^2; 3–10 cm: median, 9.9 hours; 5th, 95th percentiles of the distribution, 3.8, 25.8; *P*=.7; 6–10 cm:

FIGURE 3
Labor curves by size for gestational age and parity



Labor curves for time to progress from 0—10 cm cervical dilation in women with appropriate-for-gestational age and large-for-gestational age infants were based on actual infant birthweight and further stratified by parity (nulliparity vs multiparity).

AGA, appropriate-for-gestational age; *LGA*, large-for-gestational age.

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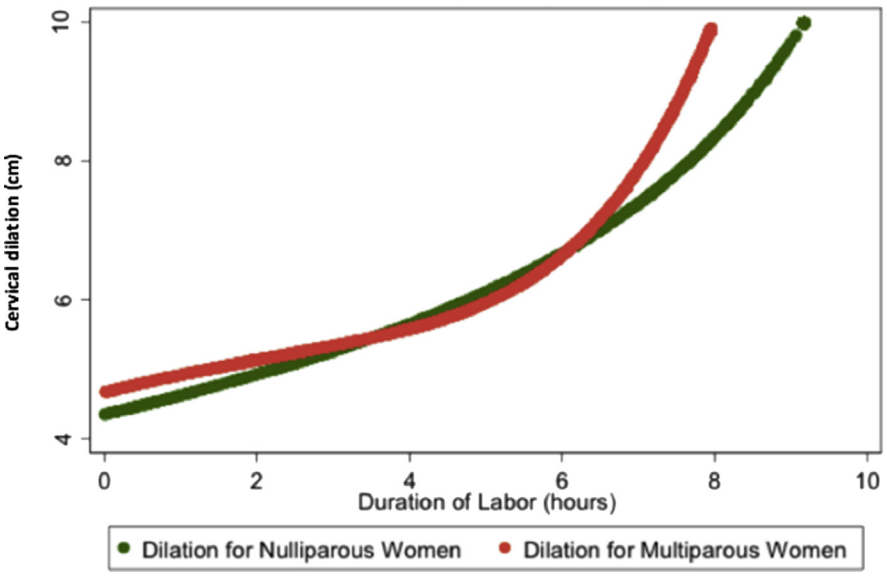
median, 2.46 hours; 5th, 95th percentiles of the distribution, 0.5, 12.2). There was a significant interaction of DM and the effect of obesity on labor progression among women with LGA infants (P=.03).

FIGURE 4
Labor curves among women with large-for-gestational age infants by parity



Labor curves for time to progress from 0—10 cm cervical dilation in women with large-for-gestational age infants were based on actual infant birthweight in nulliparous and multiparous women.

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Comment

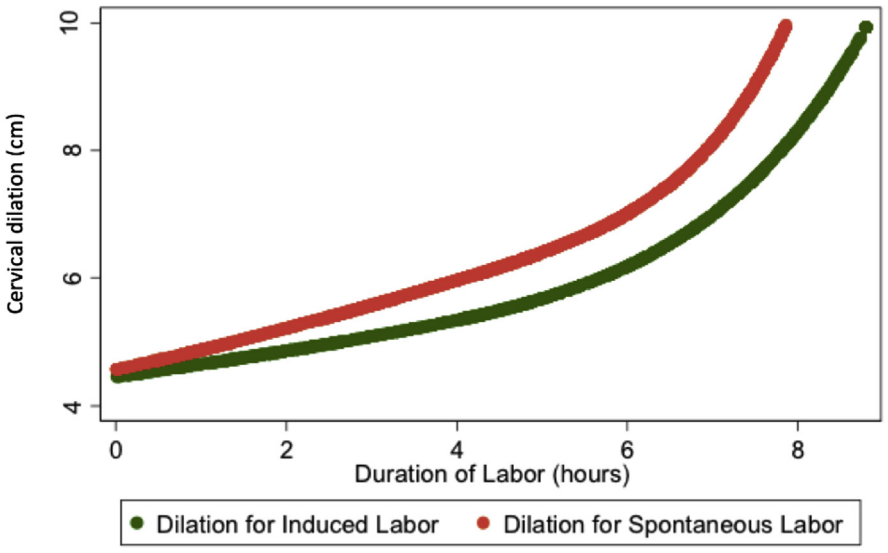
Principal findings

Among those women who complete the first stage of labor, women with LGA infants experience relatively slower labor progression compared with women with AGA infants. In our cohort, the median time to complete the first stage of labor after 3 cm was 2.1 hours longer in women with LGA infants compared with those with AGA infants. Among women with LGA infants, those who were nulliparous and obese, and presented with spontaneous labor onset but required labor augmentation with oxytocin experienced overall longer times to complete the active phase of the first stage of labor compared with their multiparous, nonobese, non-augmented counterparts. No significant difference in duration of active labor was detected among women with induced vs spontaneous labor onset. The probability value for labor duration from 3—10 cm according to type of labor onset for spontaneous vs induced labor, however, is borderline and approaches the threshold for P<.05; it is thus possible that we may be underpowered by our study sample size to detect a statistically significant difference for labor duration according to induced vs spontaneous labor onset among LGA infants. Finally, the presence of DM/GDM did not prolong labor duration in both obese and not obese women with LGA infants, both during the active phase of labor from 6—10 cm and for overall duration of the first stage of labor after 3 cm.

Results

We demonstrate that, when DM/GDM was present with obesity, the relationship between obesity and prolonged active phase of labor in the first stage in women with LGA infants was no longer significant. The significant interaction detected between DM and obesity confirms obesity and DM/GDM do not have an additive effect on the relationship between having an LGA infant and labor progression. A biologically important interaction is occurring among obese

FIGURE 5
Labor curves among women with large-for-gestational age infants by type of labor onset



Labor curves for time to progress from 0—10 cm cervical dilation in women with large-for-gestational age infants were based on actual infant birthweight in induced and spontaneously laboring women.

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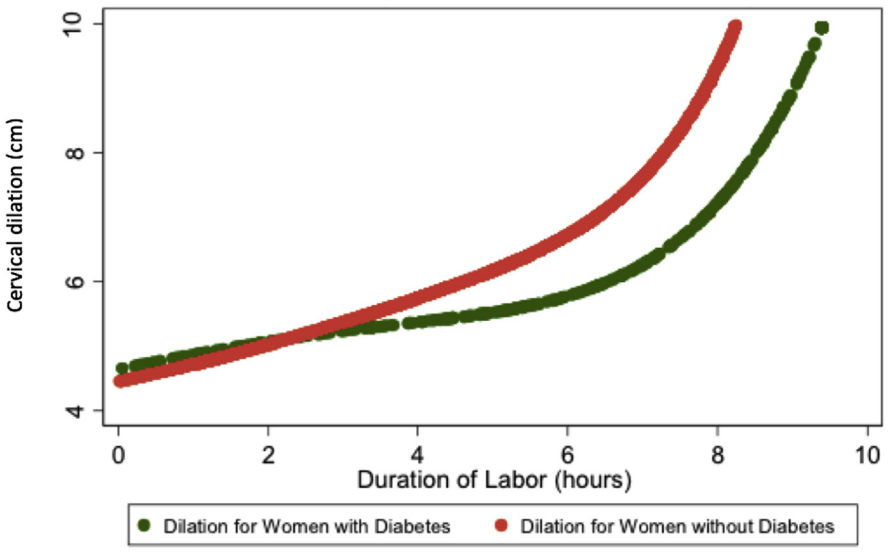
FIGURE 6
Labor curves among women with large-for-gestational age infants by maternal diabetes mellitus status



Labor curves for time to progress from 0—10 cm cervical dilation in women with large-for-gestational age infants were based on actual infant birthweight in women with and without diabetes mellitus.

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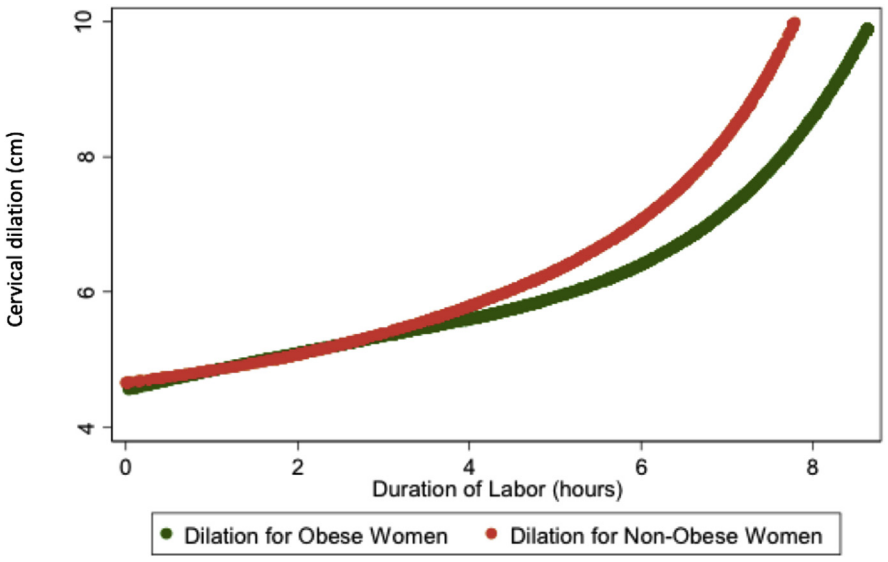
and diabetic women, because obesity increases a woman's risk of DM. However, our interaction test suggests that it is more likely that the greater adipose tissue deposits in the pelvis with weaker uterine myometrium contractility predisposes obese women to slower progression of labor, as supported by previous literature, and is less likely that the metabolic changes are associated with DM that influence labor progression.[15,25] Despite the large sample size in our overall study population, we are limited in the ability to detect statistical significance with regard to DM/GDM, given the small number of pregnant women with both LGA infants and DM/GDM in our sample (n=158).

Our results validate previous work by Dr Emanuel Friedman[16—19] in the 1950s—1970s who similarly demonstrated significant prolongations in the active phase of labor among nulliparous and multiparous women who deliver infants with increased birthweight. However, our study provides a more modern update to his early labor curves. We redefine median labor duration after 3 cm in the contemporary era according to infant size, because Zhang et al[15] and Loughton et al[26] have shown that contemporary populations do not demonstrate a consistent pattern of the active phase of labor, that they progress more gradually than was demonstrated in Friedman's early work, and yet may still achieve completion of the first stage of labor. We also expand on previous work by investigating further how other maternal factors, besides parity, influence labor progression that is specific to the LGA population. Previous studies have identified that increasing BMI is associated with slower overall first stage labor progression from 4—10 cm in the general population of women.[20,27] Among women with LGA infants, we found that the first stage of labor for obese women was of a longer median duration in the active phase, but not overall from 3—10 cm, compared with their nonobese counterparts. We further validate previous findings by Timofeev et al[28] that women with and without DM/GDM have similar labor

FIGURE 7
Labor curves among women with large-for-gestational age infants by maternal obesity status



Labor curves for time to progress from 0—10 cm cervical dilation in women with large-for-gestational age infants were based on actual infant birthweight in obese and nonobese women.

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curves when matched for maternal BMI and infant birthweight; however, the population by Timofeev et al included only spontaneous laborers, whereas we include both induced and spontaneously laboring pregnant women and control for type of labor onset in our analysis of women with DM/GDM specific to the LGA population.

Strengths and limitations

Our study is strengthened by the use of a large contemporary cohort of women at a tertiary care center with consecutive term births who reached 10 cm of cervical dilation to analyze the first stage of labor after 3 cm in women with LGA infants. Detailed extraction of patient data, including baseline demographics and labor variables, enabled us to reconstruct labor curves while adjusting for potential confounding factors. The use of an existing dataset from a single tertiary care center with similar active labor management practice patterns among providers limits the differing clinical approaches that are inherent to treating women in labor.

This study is not without limitations. By excluding women who did not complete the first stage of labor, albeit a minority of women with similar proportions in both the AGA and LGA groups, we introduce potential selection bias because the women who were excluded may have had a protraction or arrest disorder, and thereby longer labor curves, leading to cesarean delivery. However, their exclusion supported our objective to determine the normal course for the first stage of labor after 3 cm in women with LGA infants. In addition, the study design relies on typical labor management at our institution where resident physicians perform serial cervical examinations approximately every 2 hours. Our analysis is thus dependent on cervical examination data recorded at these set intervals, although interval-censored regression accounts for limitations in the use of the labor data with which we are unable to determine the precise time a cervical dilation is achieved.

We are unable to comment on labor progression from time of onset of spontaneous labor with regular painful contractions to time of presentation for admission for labor; the cervical dilation at which they present for admission is the first opportunity to capture and thereafter analyze rates of labor progression. Additionally, we cannot comment on labor progression before 3 cm of cervical dilation, because the majority of women presented for admission with advanced cervical dilation. Therefore, we cannot define the duration of latent labor in its entirety. By excluding data from the onset of labor to 3 cm, we shorten the median latent phase data for those 37% of women who presented before 3-cm cervical dilation. Similar to previous studies, the precision of our estimates of labor curve comparisons and thereby the reliability of our statistical models is reduced with respect to cervical dilation before 3 cm, given a limited number of observations at these earlier dilations; as such, data from before 3-cm dilation were excluded.[20,21,27] In addition, by summarily including pregnant women with late arrivals after the onset of labor who had already progressed >3-cm dilation, we further shorten the overall reported median duration of labor from 3—10 cm.

Clinical and research implications

Use of a reverse stepwise approach with interval-censored regression to construct labor curves backwards starting from 10 cm is difficult to translate to real-world management of labor with forward progression in clinical practice. However, this controversial method established by Zhang et al[15] is the most effective method of statistical analysis that we can use to quantify labor progression when laborers present at variable cervical dilations and when the exact timing of cervical progression before admission for labor is unknown. Given the retrospective study design, we can establish only the relationship between infant size and progression of the first stage of labor after 3 cm, but not causality. Estimations of fetal weight were not available for most patients, whether based on physician assessment via Leopold's maneuvers on admission

TABLE 4
Time to achieve 10-cm cervical dilation after 3 and 6 cm in women with large-for-gestational age infants according to diabetes mellitus/gestational diabetes mellitus and obesity status

Cervical dilation, cm	No diabetes mellitus/ gestational diabetes mellitus and normal weight (body mass index, <30 kg/m^2; n=357)	Both diabetes mellitus/ gestational diabetes mellitus and obesity (body mass index, ≥30 kg/m^2; n=124)	Diabetes mellitus/gestational diabetes mellitus alone (normal weight, body mass index, <30 kg/m^2; n=34)	Obesity alone (body mass index, ≥30 kg/m^2 and no diabetes mellitus/gestational diabetes mellitus; n=739)
3–10, hr	5.4 (2.0, 14.5)	9.9 (3.7, 26.4)	6.3 (2.4, 16.9)	9.1 (3.4, 24.3)
P value[a]	Reference	.8	.4	.3
6–10, hr	1.8 (0.4, 8.1)	2.3 (0.5, 10.6)	2.7 (0.6, 12.6)	2.3 (0.5, 10.7)
P value[a]	Reference	.07	.07	.01

Note: Data are given as median hours (5th, 95th percentiles of the distribution), adjusted for race, parity, labor onset, Bishop score ≥5 at admission, and previous cesarean delivery.

[a] Based on nonobese women without diabetes mellitus/gestational diabetes mellitus as reference group.

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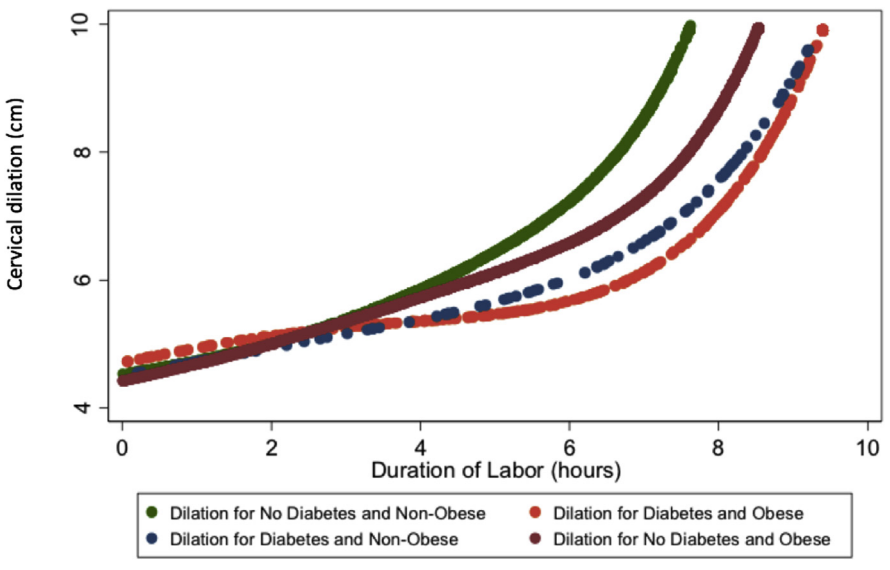
for labor or recent ultrasound measurement of fetal growth. Although only measures of estimated fetal weight are available for clinicians to guide intrapartum treatment of LGA infants, conducting our analysis based on postnatal infant birthweight allows us to identify the true biologic effect of fetal size on labor progression. Future studies should evaluate labor progression by estimated fetal weight when fetal macrosomia is suspected antenatally because this would provide greater clinical insight into anticipated labor progression, influence prospective labor management in cases of suspected fetal macrosomia, and enable comparison with our labor curves that were constructed from postnatal infant birthweight. Future studies should also evaluate the effect of pelvic shape, fetal position, and uterine infection (eg, chorioamnionitis) on labor progression, because these data were not available for analysis in our models.

FIGURE 8
Labor curves among women with large-for-gestational age infants by maternal diabetes mellitus and obesity status



Labor curves for time to progress from 0–10 cm cervical dilation in women with large-for-gestational age infants were based on actual infant birthweight in women with or without diabetes mellitus and/or obesity.

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Conclusion

We demonstrate that, among women with LGA infants, type of labor onset (induced vs spontaneous) and presence of DM/GDM do not significantly impact the time that is required to complete the first stage of labor after 3 cm dilation. However, we identify that the time required to reach the second stage of labor is greater in women with LGA infants compared with those with AGA infants overall. These differences are most pronounced in women with LGA infants in the active phase of labor who are nulliparous, are obese, or require oxytocin augmentation after spontaneous labor onset. Despite limitations that are inherent to the available statistical methods, significant trends that were identified for first-stage labor duration after 3 cm dilation in our study population suggest that clinicians should have heightened awareness to manage the first stage of labor proactively in nulliparous women, obese women, and women with LGA infants who require oxytocin augmentation after spontaneous labor onset. ■

References

1. Sadeh-Mestechkin D, Walfisch A, Shachar R, Shoham-Vardi I, Vardi H, Hallak M. Suspected

macrosomia? Better not tell. Arch Gynecol Obstet 2008;278:225–30.
2. American College of Obstetricians and Gynecologists. Fetal macrosomia: Practice Bulletin No. 173. Obstet Gynecol 2016;128:e195–209.
3. Scott A, Moar V, Ounsted M. The relative contribution of different maternal factors in large-for-gestational-age pregnancies. Eur J Obstet Gynecol Reprod Biol 1982;13:269–77.
4. Levine AB, Lockwood CJ, Brown B, et al. Sonographic diagnosis of the large for gestational age fetus at term: does it make a difference? Obstet Gynecol 1992;79:55–8.
5. Boulet SL, Alexander GR, Salihu HM, Pass M. Macrosomic births in the United States: determinants, outcomes, and proposed grades of risk. Am J Obstet Gynecol 2003;188:1372–8.
6. Barber EL, Lundsberg LS, Belanger K, Pettker CM, Funai EF, Illuzzi JL. Indications contributing to the increasing cesarean delivery rate. Obstet Gynecol 2011;118:29–38.
7. Cheng ER, Declercq ER, Belanoff C, Stotland NE, Iverson RE. Labor and delivery experiences of mothers with suspected large babies. Matern Child Health J 2015;19:2578–86.
8. Simhayoff N, Sheiner E, Levy A, Hammel RD, Mazora M, Hallaka M. To induce or not to induce labor: a macrosomic dilemma. Gynecol Obstet Invest 2004;58:121–5.
9. Friesen CD, Miller AM, Rayburn WF. Influence of spontaneous or induced labor on delivering the macrosomic fetus. Am J Perinatol 1995;12:63–6.
10. Leaphart WL, Meyer MC, Capeless EL. Labor induction with a prenatal diagnosis of fetal macrosomia. J Matern Fetal Med 1997;6:99–102.
11. Sanchez-Ramos, Bernstein LS, Kaunitz AM. Expectant management versus labor induction for suspected fetal macrosomia: a systematic review. Obstet Gynecol 2002;100:997–1002.
12. Moldéus K, Cheng YW, Wikström AK, Stephansson O. Induction of labor versus expectant management of large-for-gestational-age infants in nulliparous women. PLoS One 2017;12:e0180748.
13. Hamilton BE, Hoyert DL, Martin JA, Strobino DM, Guyer B. Annual summary of vital statistics: 2010-2011. Pediatrics 2013;131:548–58.
14. American College of Obstetricians and Gynecologists, Society for Maternal-Fetal Medicine, Caughey AB, Cahill AG, Guise JM, Rouse DJ. Safe prevention of the primary cesarean delivery. Am J Obstet Gynecol 2014;210:179–93.
15. Zhang J, Landy HJ, Branch DW, et al. Contemporary patterns of spontaneous labor with normal neonatal outcomes: Consortium on Safe Labor. Obstet Gynecol 2010;116:1281–7.
16. Friedman EA. The graphic analysis of labor. Am J Obstet Gynecol 1954;68:1568–75.
17. Friedman EA. Primigravid labor: a graphicostatistical analysis. Obstet Gynecol 1955;6:567–89.
18. Friedman EA, Sachtleben MR. Preterm labor. Am J Obstet Gynecol 1969;104:1152–8.
19. Friedman EA. Labor: clinical evaluation and management, 2nd ed. New York: Appleton-Century-Crofts; 1978.
20. Norman SM, Tuuli MG, Odibo AO, Caughey AB, Roehl KA, Cahill AG. The effects of obesity on the first stage of labor. Obstet Gynecol 2012;120:130–5.
21. Harper LM, Caughey AB, Odibo AO, Roehl KA, Zhao Q, Cahill AG. Normal progress of induced labor. Obstet Gynecol 2012;119:1113–8.
22. Duryea EL, Hawkins JS, McIntire DD, Casey BM, Leveno KJ. A revised birth weight reference for the United States. Obstet Gynecol 2014;124:16–22.
23. Klein JP, Moeschberger ML. Survival analysis: techniques for censored and truncated data. Berlin: Springer; 1997.
24. Vahratian A, Troendle JF, Siega-Riz AM, Zhang J. Methodological challenges in studying labor progression. Paediatr Perinat Epidemiol 2006;20:72–8.
25. Crowder KJ, Hand DJ. Analysis of repeated measures. New York: Chapman and Hall; 1990.
26. Loughton SK, Branch DW, Beaver J, Zhang J. Changes in labor patterns over 50 years. Am J Obstet Gynecol 2012;206:419.e1–9.
27. Kominiarek MA, Zhang H, VanVeldhuisen P, Troendle J, Beaver J, Hibbard JU. Contemporary labor patterns: the impact of maternal body mass index. Am J Obstet Gynecol 2011;205:244.e1–8.
28. Timofeev J, Huan CC, Singh J, Driggers RW, Landy HJ. Spontaneous labor curves in women with pregnancies complicated by diabetes. J Matern Fetal Neonatal Med 2012;25:20–6.

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