Published online: 09.08.2019

Serial Cervical Length Evaluation in Low-Risk Women with Shortened Cervical Lengths in the Midtrimester: How Many Will Dilate Prior to 24 Weeks?

Kelly B. Zafman, MD, MSCR[1] Andrei Rebarber, MD[2,3] Nathan S. Fox, MD[2,3]

[1] Department of Obstetrics, Gynecology, and Reproductive Science, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania
[2] Department of Obstetrics, Gynecology, and Reproductive Science, Icahn School of Medicine at Mount Sinai, New York, New York
[3] Maternal Fetal Medicine Associates, PLLC, New York, New York

Address for correspondence Kelly B. Zafman, MD, MSCR, Hospital of the University of Pennsylvania, 3400 Spruce Street, Philadelphia, PA 19146 (e-mail: kelly.zafman@gmail.com).

Am J Perinatol 2020;37:14–18.

Abstract

Objective To determine what proportion of women with a short cervical length (CL) without a history of spontaneous preterm birth (SPTB) will ultimately be dilated at <24 weeks.

Study Design This is a retrospective cohort study of women with singleton pregnancies with a short CL (≤25 mm) between 16 and 22 weeks' gestational age (GA). We excluded women with a history of SPTB. We examined the progression of women with short CL based on the CL measurement and GA at diagnosis. The primary outcome was cervical dilation or spontaneous delivery <24 weeks.

Results A total of 163 women were included, of whom 27 (16.6%) were ultimately dilated and 4 (2.5%) had pregnancy loss by 24 weeks. The median GA at diagnosis of short CL was $19^{5/7}$ (range: 15–22) weeks. Women with a CL <15 mm were more likely to have cervical dilation or loss prior to 24 weeks than women whose CL was 15 to 25 mm (42.5 vs. 11.9%, <0.001, adjusted odds ratio: 3.72, 95% confidence interval: 1.52–9.09). GA at diagnosis was not associated with risk of progression.

Conclusion In women with a short CL without a history of SPTB, the risk of dilation or pregnancy loss <24 weeks is significant, approaching 50% for women with a CL <15 mm.

Keywords
- cervical length
- short cervix
- preterm birth

In the United States, spontaneous preterm birth (SPTB) complicates more than 1 out of 10 pregnancies and remains one of the most common causes of neonatal morbidity and mortality.[1] Cerclage placement has been a common practice to help prolong gestation and decrease the risk of SPTB. The decision to place a cerclage is made based on a woman's obstetrical history, cervical length (CL) on ultrasound exam, and/or cervical dilation on physical exam.[2] While there is strong evidence on the benefit of cerclage in women with a history of SPTB and short CL,[3] the management of women with an early short cervix without a history of SPTB continues to be debated.

For women with a short cervix found incidentally on ultrasound exam, there are a few possible interventions that may be offered. Current evidence supports offering vaginal progesterone to women with a CL ≤25 mm, as vaginal progesterone in this population significantly decreases the risk of SPTB as well as the risk of poor neonatal outcomes.[4] The benefit of pessary placement in women with

received
May 28, 2019
accepted
June 25, 2019
published online
August 9, 2019

Copyright © 2020 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA.
Tel: +1(212) 584-4662.

DOI https://doi.org/10.1055/s-0039-1694006.
ISSN 0735-1631.

Downloaded by: Icahn School of Medicine at Mount Sinai. Copyrighted material.

a short CL and no history of SPTB is not as clear with inconsistent findings across recent studies.[5–7] Finally, there is good evidence that routine cerclage placement in women with a short CL without a history of SPTB is not beneficial; it exposes women to the risks of the procedure without decreasing the risk of SPTB.[8]

In contrast to women with a short CL, women with a dilated cervix do appear to benefit from cerclage.[9] It is not well understood, however, which women with a short CL will ultimately become dilated, nor is it known whether serial CL assessment after the initial diagnosis of a short CL is beneficial. In our practice for women with a short CL and no history of SPTB, we recommend vaginal progesterone (as well as sometimes a pessary), but we also continue to do serial CLs to assess the cervix for progressive shortening and dilation. If there is significant change in CL, we perform a speculum exam to assess for cervical dilation. Then, if the cervix is dilated $<$24 weeks, we typically recommend cerclage.

The objective of this study was to determine what proportion of women with a short CL without a history of SPTB will ultimately have cervical dilation prior to $<$24 weeks and thus be candidates for a cerclage. We also sought to determine if there were any risk factors in women with a short CL that could predict cervical dilation prior to 24 weeks. This information could help providers better counsel their patients and plan for follow-up CLs or exams prior to 24 weeks.

Materials and Methods

This was a retrospective cohort study of all women who presented to a single maternal–fetal medicine ultrasound unit from January 2011 to May 2018. We included women with a singleton pregnancy and no prior SPTB who had a short CL measurement, defined as $\leq$25 mm, between 16 and 22 weeks' gestational age (GA).

We excluded women with multifetal gestations and women with a history of SPTB, as women with SPTB were routinely offered cerclage at the time that the short CL was discovered.[3] We also excluded women who had a cerclage placed before 16 weeks. Finally, we excluded women who received a cerclage for any reason before they had cervical dilation (although we do not recommend cerclage until there is cervical dilation, some of the referring obstetricians place cerclages based on different criteria).

Over the course of the study period, our practice guidelines did not change. All women were screened with a transabdominal CL during routine ultrasound examination of fetal anatomy. A transabdominal CL $<$35 mm was considered suspicious for a short cervix. At this point, a transvaginal CL measurement was recommended. Besides a short transabdominal CL, indications for transvaginal CL screening in our practice include history of cervical cone biopsy, loop electrosurgical excision procedure (LEEP), uterine anomaly, or women with symptoms such as contractions, abdominal pressure, or bleeding. Our practice does not perform universal transvaginal CL screening in singleton pregnancies; however, if a referring provider requests a transvaginal CL measurement in an asymptomatic woman without indications, CL measurement is performed.

Upon diagnosis of a short CL, all women were recommended to initiate vaginal progesterone. Pessary was recommended for some patients based on the provider's clinical judgment and patient preference. After diagnosis of a short CL, women were recommended to undergo serial CL measurements at least every 2 weeks. Speculum exam was performed if the CL was less than 10 mm or the cervix appeared dilated on ultrasound. Cerclage was offered for women who were found to have a dilated cervix on physical exam, assuming there were no contraindications to the procedure.

All CL measurements were done in an outpatient setting on asymptomatic patients. All tests done in labor and delivery were excluded because they were done on symptomatic patients as part of a preterm labor evaluation.

The GA was based on the last known menstrual period or by in vitro fertilization dating and confirmed by first-trimester sonography in all patients. Monoamniotic twins were excluded, as were pregnancies with aneuploidy or major fetal anomalies discovered before or after birth. Patients with a cerclage placed before 16 weeks were excluded from analysis. Patients and obstetricians were not blinded to the CL measurements. In our practice, we do not routinely tocolyze or hospitalize asymptomatic patients with a short cervix. On the basis of the CL and GA, we may consider administering steroids. We only tocolyze or hospitalize patients who are considered to be in acute preterm labor.

As we were examining CLs at different GAs, we defined a short CL as any CL at or below the 10th percentile for that GA. We also analyzed our data defining a short CL as 25 mm or less, which is commonly used as a definition for a short CL. We looked at CL measurements in four second-trimester GA ranges: 16 to $17^{6/7}$, 18 to $19^{6/7}$, 20 to $21^{6/7}$, and 22 to $23^{6/7}$ weeks. Most of our twin pregnancies have more than one CL measurement between 16 and $23^{6/7}$ weeks. However, as we evaluated each 2-week window separately and did not combine CL measurements from different 2-week windows, we did not adjust for multiple measurements in the same patient. If any patient had two CL measurements within one 2-week window, the first CL measurement in that window was used for analysis.

Our protocol for CL measurement has been previously described.[10] Briefly, CL measurements were done in an outpatient setting. All CL measurements were measured by 4- to 8-MHz transvaginal probes (LOGIQ a200 and Voluson 530 and 730 Expert; GE Healthcare, Milwaukee, WI) with an empty bladder and with the optimal image defined according to the criteria reported by Iams et al.[11] The shortest functional CL was used because this has been found to be the most reproducible measurement.[12] The GA was based on the last known menstrual period or by in vitro fertilization (IVF) dating and confirmed by first-trimester ultrasound in all patients. Patients and obstetricians were not blinded to the CL measurements. In our practice, we do not routinely tocolyze or hospitalize asymptomatic patients with a short cervix.

For each patient, we reviewed the computerized medical record and ultrasound reports. We recorded maternal

Downloaded by: Icahn School of Medicine at Mount Sinai. Copyrighted material.

baseline characteristics, ultrasound data, and delivery information. We examined the progression of women with short CLs between 16 and 22 weeks' GA based on the CL measurement. Our primary outcome was cervical dilation prior to 24 weeks or pregnancy loss prior to 24 weeks. We categorized the CLs into two groups: <15 and 15 to 25 mm. We reported the CL measurements in two intervals: 16 to $19^{6/7}$ and 20 to 22 weeks. If women underwent more frequent CL measurements, we used the first measurement in that interval. If a woman had a cerclage placed, she was excluded from all subsequent CL measurements.

We first compared baseline characteristics of women with and without the primary outcome using chi-square test and Student's *t*-test as appropriate (IBM SPSS for Windows 22.0, IBM Corp.). We then compared the likelihood of the primary outcome based on the initial CL at the time of diagnosis of a short CL, as well as the GA. A *p*-value of <0.05 was considered significant. For all baseline characteristics that differed ($p < 0.05$) between women with and without the primary outcome, we performed a regression analysis to identify which risk factors were independently associated with the primary outcome.

Results

A total of 163 women met inclusion criteria, of whom 27 (16.6%) were ultimately dilated and 4 (2.5%) had a pregnancy loss by 24 weeks' GA. Baseline characteristics of these women are shown in ►Table 1. Women who were ultimately dilated or had a pregnancy loss at <24 weeks were more likely to have conceived by IVF (29.0 vs. 12.9%, $p = 0.03$), have a shorter CL at the first diagnosis of short cervix (14.7 vs. 19.4 mm, $p < 0.001$), and have no history of cone/LEEP (6.5 vs. 29.5%, $p = 0.008$). The most common indication for CL measurement in both groups was routine screening.

Overall, 46 (28.2%) women had a cerclage placed between 16 and 24 weeks' GA. Of the women who received a cerclage, 20 (48.9%) had the cerclage placed only once they were found to be dilated, while 26 (51.1%) women had the cerclage placed for the indication of short CL alone. Twenty-nine (17.8%) women had a pessary placed.

The risk of dilation or pregnancy loss at <24 weeks by initial CL and GA is shown in ►Table 2. The risk of cervical dilation or pregnancy loss prior to 24 weeks was high, and significantly higher in the women whose CL was <15 mm (41.7 vs. 12.6%, $p < 0.001$). There was a significantly increased risk of dilation or pregnancy loss when CL was <15 mm compared with 15 to 25 mm both at 16 to $19^{6/7}$ weeks (43.8 vs. 11.4%, $p = 0.01$) and 20 to 22 weeks (40.0 vs. 13.0%, $p < 0.001$). There was no significant difference in the risk of dilation or pregnancy loss by the GA at the time of short CL.

We performed a logistic regression to determine the odds of dilation or pregnancy loss by <24 weeks' GA by the initial short CL and the GA at the first short CL, adjusting for differences in baseline characteristics (►Table 3). On univariate analysis, a CL <15 mm and IVF were associated with significantly higher odds of dilation or pregnancy loss, while a history of cone/LEEP was associated with a decreased risk of dilation or pregnancy loss. GA at first CL was not significantly associated with dilation or pregnancy loss. These relationships remained true on adjusted analysis; a CL <15 mm and IVF were independently associated with an increased risk of dilation or pregnancy loss, while a history of cone/LEEP was independently associated with a decreased risk.

Finally, we performed an exploratory analysis comparing the outcomes for women who received a cerclage prior to dilation with those who received a cerclage only once the cervix was found to be dilated (►Table 4). There were no significant differences between the groups for the baseline CL and GA at the first short CL. Outcomes also did not differ between the groups.

Table 1 Background characteristics of women who were ultimately dilated or had pregnancy loss <24 weeks versus not dilated

Demographics	Not dilated prior to 24 wk ($n = 132$)	Dilated or pregnancy loss prior to 24 wk ($n = 31$)	*p*-Value
Age (y)	34.9 ± 4.8	35.7 ± 6.3	0.47
Prepregnancy obesity	11 (8.3%)	4 (12.9%)	0.43
White race	81 (61.8%)	20 (64.5%)	0.82
Fibroids	21 (15.9%)	6 (19.4%)	0.64
In vitro fertilization	17 (12.9%)	9 (29.0%)	0.03
Gestational age at first CL	19.9 ± 1.6	19.5 ± 2.6	0.16
Initial short CL (mm)	19.4 ± 4.9	14.7 ± 6.3	<0.001
Indication for cervical length			
History of cervical cone/LEEP	39 (29.5%)	2 (6.5%)	0.008
Uterine anomaly	8 (6.1%)	0 (0.0%)	0.36
Symptomatic	9 (6.8%)	5 (16.1%)	0.10
Suspected short	8 (6.1%)	4 (12.9%)	0.19
Done routinely	68 (51.5%)	20 (64.5%)	0.19

Abbreviations: CL, cervical length; LEEP, loop electrosurgical excision procedure.
Note: Data presented as mean ± standard deviation or *n* (%).

Table 2 Percentage of women who were ultimately dilated or had a pregnancy loss <24 weeks' GA

Initial cervical length	<15 mm ($n = 36$)	15–25 mm ($n = 127$)	*p*-Value
All women	15/36 (41.7)	16/127 (12.6)	<0.001
16–20 wk GA[a]	7/16 (43.8)	4/35 (11.4)	0.01
20–22 wk GA	8/20 (40.0)	12/92 (13.0)	<0.001

Abbreviation: GA, gestational age.
[a]Fifteen women had cerclages placed <20 weeks.

Downloaded by: Icahn School of Medicine at Mount Sinai. Copyrighted material.

Table 3 Odds of ultimately being dilation <24 weeks by CL

	OR (95% CI)	aOR (95% CI)
Initial CL		
15–25 mm	Ref.	Ref.
< 15 mm	4.96 (2.13–11.53)	3.72 (1.52–9.09)
GA at first short CL		
20–24 wk	Ref.	Ref.
16–20 wk	0.79 (0.35–1.80)	1.02 (0.41–2.54)
In vitro fertilization	2.77 (1.09–7.00)	2.83 (1.02–7.81)
History of cone/LEEP	0.16 (0.04–0.70)	0.21 (0.04–0.96)

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; CL, cervical length; GA, gestational age; LEEP, loop electrosurgical excision procedure.

Table 4 Outcomes for women who received cerclage before dilation versus women who received cerclage at dilation

	Cerclage prior to dilation ($n = 20$)[a]	Cerclage at dilation ($n = 18$)[b]	*p*-Value
Baseline CL (mm)	16.8 ± 6.2	17.0 ± 5.5	0.46
GA at first short CL	19.0 ± 1.7	19.8 ± 1.5	0.08
Delivery <37 wk	10 (50.0%)	5 (27.8%)	0.16
Delivery <34 wk	2 (10.0%)	3 (16.7%)	0.54
Delivered <28 wk	1 (5.0%)	2 (11.1%)	0.46
Delivered <24 wk	1 (5.0%)	1 (5.6%)	0.73

Abbreviations: CL, cervical length; GA, gestational age.
[a]Six records not available.
[b]Two records not available.

Comment

In this study, we found that among women with a short cervix and no history of SPTB, the risk of dilation or pregnancy loss at <24 weeks is significant. Almost half of the women with a CL <15 mm ultimately were dilated or had pregnancy loss, both when CL was <15 mm at 16 to $19^{6/7}$ weeks (43.8%) and at 20 to 22 weeks (41.7%). A CL <15 mm was associated with a fourfold higher risk of ultimately being dilated or pregnancy loss compared with a CL 15 to 25 mm, even after controlling for differences in baseline characteristics between the groups. IVF increased the risk of ultimately being dilated or having a pregnancy loss, while a history of cervical cone or LEEP was protective. When we examined a subset of women who got a cerclage placed before they were dilated (for the indication of short CL alone), we found no significant differences in the rates of preterm birth compared with women who got a cerclage placed only after becoming dilated.

Previous studies have established that even in the absence of a history of SPTB, a short CL in singleton pregnancies significantly increases the risk of preterm delivery. For these women with a CL ≤25 mm, a recent meta-analysis found that cerclage does not decrease the risk of preterm delivery or adverse neonatal outcomes except in women with the shortest CLs.[8] In this meta-analysis, cerclage was found to reduce the incidence of SPTB <35 weeks for women with a CL <10 mm (relative risk = 0.68; 95% confidence interval: 0.47–0.98).[8] We suspect the reason cerclage might be beneficial in this cohort is that either many of them actually have a dilated cervix when the CL is <10 mm, or as many of them will ultimately become dilated, as we found in our study. In our study, almost half of women with a CL <15 mm either become dilated or had a pregnancy loss <24 weeks. This supports the practice of not only following the CL with serial exams for these women, but also considering cerclage as an option for women with the shortest CLs.

In addition to shorter CL as a predictor for ultimately being dilated <24 weeks, IVF was also found to be associated with a higher risk of dilation. In a study of diamniotic twins who underwent routine CL screening, Saccone et al found that twins conceived by IVF had a significantly shorter CL than twins conceived spontaneously (32.2 ± 10.5 vs. 34.1 ± 9.1 mm) and a higher risk of SPTB ≤34 weeks (32.9 vs. 21.2%).[13] We found that IVF was independently associated with dilation or pregnancy loss <24 weeks in singleton pregnancies with a short cervix, even after for controlling for CL at the initial short CL diagnosis. Saccone et al suggested women who conceived by IVF are more likely to have undergone invasive procedures such as hysteroscopy or uterine evacuation than those who conceived spontaneously. These procedures have previously been shown to be associated with shorter CLs and increased risk of SPTB.[13] While a prospective study is needed, our data may suggest that in practices that do not perform universal CL measurements in asymptomatic singletons without a history of SPTB, IVF may be an indication for screening for short CL in this population.

In contrast, we found that a history of cervical cone or LEEP was protective for dilation or pregnancy loss <24 weeks. In our practice, we routinely screen these women for short CL at 16 weeks, as women with a history of these cervical procedures have a higher risk of second trimester loss. CL has been found to be associated with SPTB in this population of women.[14] It is possible that we found a lower risk of dilation in these women because our population was restricted to those women without a history of SPTB. The women included in our cohort may, therefore, represent a lower risk group of women who have a history of cone/LEEP since they did not deliver preterm in a prior pregnancy.

Finally, we found that women who received a cerclage prior to dilation (for the indication of short CL alone, by outside providers as we do not recommend this) had no better outcomes than women who did not receive a cerclage until they were dilated. It is likely that some of the women who had a cerclage placed would not have ultimately been dilated, representing a group of women that does not typically benefit from cerclage placement. There has been some retrospective data to suggest that women with extremely shortened CL (≤10 mm) and no history of SPTB may have improved outcomes with

Downloaded by: Icahn School of Medicine at Mount Sinai. Copyrighted material.

cerclage placement.[8,15] Our data suggest that routine cerclage prior to dilation in women with a CL $\leq$25 mm does not decrease the risk of SPTB. This supports the practice of performing serial CLs in women with a short cervix and potentially offering cerclage only if the cervix is dilated.

Our study is limited by its retrospective design. Our practice does not perform routine vaginal CLs in asymptomatic women without a history of SPTB unless requested by a referring provider, so about half of the women included in our study had risk factors for short CL. It is possible that our cohort is at higher risk of short cervix (and consequently, dilation) than a practice that does universal CL screening. Additionally, our study may be limited by the homogeneous population. Though using data from one practice limited the number of women in this analysis, and reduces the heterogeneity of the population, we believe it increases the reliability of the data as there was a standardized protocol for CL testing, which occurred at a single ultrasound unit with maternal–fetal medicine specialists reviewing the findings. Finally, as our ultrasound unit is a referral center, we did not have access to delivery information for all patients. Our data on the GA at delivery in this population are limited by the missing records, and we were likely underpowered to detect differences in rates of preterm delivery based on timing of cerclage placement.

In conclusion, in women with a short CL without a history of SPTB, the risk of dilation or pregnancy loss <24 weeks is significant, approaching 50% for women with a CL <15 mm. The risk of dilation increases with a shorter CL but is not associated with the GA that the short cervix is identified. Routine cerclage placement prior to dilation is not associated with improved outcomes compared with waiting until the cervix is found to be dilated. We believe these data support the practice of serial CLs in women found to have a short CL to identify those who ultimately become dilated and can be offered cerclage.

Note

This study was presented as a poster at the Annual Scientific Meeting of the Society for Maternal-Fetal Medicine, February 15–17, 2019, Las Vegas, NV.

Conflict of Interest

None declared.

References

1 Martin JA, Hamilton BE, Osterman MJK. Births in the United States, 2017. NCHS Data Brief 2018(318):1–8

2 Alfirevic Z, Stampalija T, Medley N. Cervical stitch (cerclage) for preventing preterm birth in singleton pregnancy. Cochrane Database Syst Rev 2017;6:CD008991

3 Owen J, Hankins G, Iams JD, et al. Multicenter randomized trial of cerclage for preterm birth prevention in high-risk women with shortened midtrimester cervical length. Am J Obstet Gynecol 2009;201(04):375.e1–375.e8

4 Hassan SS, Romero R, Vidyadhari D, et al; PREGNANT Trial. Vaginal progesterone reduces the rate of preterm birth in women with a sonographic short cervix: a multicenter, randomized, double-blind, placebo-controlled trial. Ultrasound Obstet Gynecol 2011; 38(01):18–31

5 Saccone G, Maruotti GM, Giudicepietro A, Martinelli P; Italian Preterm Birth Prevention (IPP) Working Group. Effect of cervical pessary on spontaneous preterm birth in women with singleton pregnancies and short cervical length: a randomized clinical trial. JAMA 2017;318(23):2317–2324

6 Saccone G, Ciardulli A, Xodo S, et al. Cervical pessary for preventing preterm birth in singleton pregnancies with short cervical length: a systematic review and meta-analysis. J Ultrasound Med 2017;36(08):1535–1543

7 Dugoff L, Berghella V, Sehdev H, Mackeen AD, Goetzl L, Ludmir J. Prevention of preterm birth with pessary in singletons (PoPPS): randomized controlled trial. Ultrasound Obstet Gynecol 2018;51 (05):573–579

8 Berghella V, Ciardulli A, Rust OA, et al. Cerclage for sonographic short cervix in singleton gestations without prior spontaneous preterm birth: systematic review and meta-analysis of randomized controlled trials using individual patient-level data. Ultrasound Obstet Gynecol 2017;50(05):569–577

9 Pereira L, Cotter A, Gómez R, et al. Expectant management compared with physical examination-indicated cerclage (EM-PEC) in selected women with a dilated cervix at 14(0/7)-25(6/7) weeks: results from the EM-PEC international cohort study. Am J Obstet Gynecol 2007;197(05):483.e1–483.e8

10 Ayodele A, Fox NS, Gupta S, et al. The association between fetal fibronectin, cervical length, and amniotic fluid sludge with histological indicators of placental inflammation in twin gestations. Am J Perinatol 2018;35(03):242–246

11 Iams JD, Goldenberg RL, Meis PJ, et al; National Institute of Child Health and Human Development Maternal Fetal Medicine Unit Network. The length of the cervix and the risk of spontaneous premature delivery. N Engl J Med 1996;334(09):567–572

12 Yost NP, Bloom SL, Twickler DM, Leveno KJ. Pitfalls in ultrasonic cervical length measurement for predicting preterm birth. Obstet Gynecol 1999;93(04):510–516

13 Saccone G, Zullo F, Roman A, et al. Risk of spontaneous preterm birth in IVF-conceived twin pregnancies. J Matern Fetal Neonatal Med 2019;32(03):369–376

14 Miller ES, Grobman WA. The association between cervical excisional procedures, midtrimester cervical length, and preterm birth. Am J Obstet Gynecol 2014;211(03):242.e1–242.e4

15 Enakpene CA, DiGiovanni L, Jones TN, Marshalla M, Mastrogiannis D, Della Torre M. Cervical cerclage for singleton pregnant patients on vaginal progesterone with progressive cervical shortening. Am J Obstet Gynecol 2018;219(04):397.e1–397.e10

Downloaded by: Icahn School of Medicine at Mount Sinai. Copyrighted material.