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Longitudinal study of quantitative changes in pelvic organ support among parous women

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Structured abstract

Background—Pelvic organ prolapse is more common among parous (versus nulliparous) women and also more common after vaginal (versus cesarean) birth. However, very little is known about how childbirth affects the course and progression of pelvic organ prolapse across a woman's lifespan.

Objective—To investigate longitudinal, quantitative changes in pelvic organ support after childbirth, focusing on the impact of vaginal versus cesarean delivery.

Study design—This was a prospective longitudinal cohort study in which parous women were recruited 5–10 years from first delivery and followed annually. Using data from annual Pelvic Organ Prolapse Quantification examinations, we considered changes in vaginal support at the anterior vaginal wall (point Ba), the vaginal apex (point C), and the posterior wall (point Bp). In univariate and multivariable models, we compared pelvic organ support between women who had delivered at least one child vaginally versus those delivered exclusively by cesarean. Other covariates considered included race, age at first delivery, and the size of the genital hiatus (GH). For models of support at Ba and Bp we also considered the independent association with apical support. For women who delivered vaginally, we also considered forceps birth.

Results—1224 women participated for a total of 7055 woman-visits. In multivariable models, vaginal birth was associated with significantly worse support 5 years from first delivery. Also, women with at least one vaginal birth had more rapid worsening of support at C. The width of GH was a significant independent predictor of worse support 5 years from delivery as well as the rate

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of change over time. In models that controlled for GH, the strength of the impact of vaginal birth was attenuated.

Conclusions—Vaginal birth was associated with worse support 5 years from first delivery and with more rapid deterioration in support at the apex. Above and beyond the impact of vaginal birth, the size of GH may be an independent marker for those at greatest risk of prolapse progression.

Introduction

In the first decade after childbirth, pelvic organ prolapse is strongly associated with vaginal (versus cesarean) birth.¹ Specifically, the odds of uterovaginal prolapse to or beyond the hymen are five times higher among women with a history of vaginal birth compared to women who have delivered by cesarean.¹

However, very little is known about how childbirth affects the course and progression of pelvic organ prolapse across a woman's lifespan. Prior studies have suggested that prolapse may progress in some women but regress in others.^{2–3} Progression of prolapse is an important concept: the mildest forms of prolapse have no impact on health or quality-of-life, while more severe cases may be associated with disabling chronic symptoms as well as major surgery. What factors contribute to the natural history of prolapse are not clear.

The objective of this study was to investigate the effect of obstetrical exposures on changes in pelvic organ support after childbirth, focusing on the impact of vaginal versus cesarean delivery.

Materials and Methods

Data were obtained from a longitudinal cohort of parous women. This observational study was approved by the institutional review board; all participants provided written informed consent. Study participants were selected by route of delivery (cesarean, vaginal) and were enrolled between 2008 and 2013. Recruitment methods, selection criteria, and exclusion criteria have been previously described.¹ At the time of recruitment, each participant was 5–10 years from first birth. After enrollment, participants were followed annually through June of 2017. Thus, at the time of analysis, a participant might have participated in as many as nine annual assessments.

Pelvic Organ Prolapse Quantification (POPQ) examination⁴ was performed at the initial visit and annually. Examiners were blinded to prior examinations, birth history, and symptoms. Each point was measured to the nearest 0.5 cm. Because focus of these analyses was change in support over time, we excluded women who attended only one visit. Using data from annual POPQ examinations, we considered changes in vaginal support at three sites: point Ba (the most dependent position of any part of the anterior vaginal wall from the apex to the point 3cm proximal to the external urethral meatus), point C (the most dependent edge of the cervix or vaginal cuff), and point Bp (the most dependent position of any part of the posterior vaginal wall from the apex to the point 3cm proximal to the hymen).

The independent variable of greatest interest in this study was route of delivery: women with at least one vaginal delivery were compared to those with only cesarean birth. For each participant, a review of her obstetrical records was used to classify route of delivery as well as forceps assisted vaginal delivery. If the obstetrical record was not available (e.g., for deliveries occurring at nonaffiliated hospitals), the woman's description of her birth was used to classify her obstetrical exposures. In the study population, agreement between maternal recall and the obstetrical record was excellent for both route of delivery ($\kappa=1.0$) and forceps delivery ($\kappa=0.85$).⁵

Other covariates were assessed at baseline and annually. Each woman's primary race was self-reported. Body mass index (BMI) was measured at each annual study visit and categorized for analyses as $< 25 \text{ kg/m}^2$ (normal weight, reference), 25 to 30 kg/m^2 (overweight) or $> 30 \text{ kg/m}^2$ (obese). Other continuous variables (age at first delivery, GH, and C) were classified into approximate tertiles (where the approximation was necessitated by the limit of measuring to nearest 0.5 cm), based on the distribution of values at the enrollment visit. For example, the size of the genital hiatus (GH), measured with Valsalva at each study visit was classified as $< 2 \text{ cm}$ (reference), 2.5 to 3 cm or $> 3.5 \text{ cm}$. Finally, for our analyses of the anterior (Ba) and posterior (Bp) vaginal walls, we controlled for support at the apex (point C), also classified into approximate tertiles: < -7 (reference), -6.5 to -5.5 or > -5 . For longitudinal analyses, the following covariates were time-varying (e.g., could change over time): obstetrical parity, BMI, GH, and point C.

In our first set of analyses, we described the rate of change, at the woman-level, of vaginal support (per five-year interval). The median rate of change (and interquartile range) were calculated. We limited this first set of analyses to participants with three or more visits because estimates produced among women with only two visits were felt to be unreliable (and a standard error for the slope was unattainable). Comparisons of the distribution of slopes of the two delivery groups were carried out by testing the equality of averages of the individuals' slopes, weighted by the inverse of the variances, excluding cases in which the inverse variances of the individuals' slopes were higher than 20 to avoid undue influence of this handful of women.

In a second set of analyses, we used linear mixed effects models to further analyze the longitudinal data collected in the full study population (including all participants with at least two visits). Covariates (e.g., vaginal versus cesarean birth) were allowed to modify the initial level of support as well as the rate of change in support (e.g., slope). Since by design the study enrolled women between 5 to 10 years from first delivery, our models began at an origin defined for each woman as the point 5 years after her first delivery. Specifically, let t_{ij} denote the number of years from the origin (defined as 5 years from first delivery) when the i^{th} woman had her j^{th} study visit. In addition, let Y_{ij} denote the level of vaginal support of the i^{th} woman at the j^{th} study visit and let Z_{ij} denote the level of a covariate of the i^{th} woman at the j^{th} visit. The univariate model therefore takes the form

$$Y_{ij} = (\alpha_0 + \alpha_1 Z_{ij} + a_i) + (\beta_0 + \beta_1 Z_{ij} + b_i) t_{ij} + e_{ij}$$

where a_i and b_i are the between-women differences from the group averages level and slope and e_{ij} are the differences of the longitudinal data of the i^{th} woman (within-woman differences). In this equation, of particular interest is whether $\alpha_1 = 0$ (i.e., no effect of covariate Z on the mean value at the origin); and whether $\beta_1 = 0$ (i.e., no effect of Z on rate of change). Statistical analyses using mixed models were conducted using the “PROC MIXED” procedure in SAS (SAS Institute, Cary, NC).

Results

The cohort included 1528 women. We excluded 296 who came for only one visit and eight who reported prolapse surgery before enrollment. Among the remaining 1224 women, followed for 2–9 years, ten women reported prolapse surgery during longitudinal follow up. For these ten women, we only included data from their annual visits up to the time of the reported surgery (e.g., data for the subsequent visits were excluded from analysis). Overall, 54 participants had a hysterectomy (16 prior to enrollment and 38 during follow-up) for indications unrelated to prolapse; data for these women were included in final analyses.

After these exclusions, the 1224 women contributed a total of 7055 woman-visits to the study. The population is described, according to characteristics at the time of study enrollment, in Table 1. Comparing women who experienced at least one vaginal birth to those who delivered exclusively by cesarean, the genital hiatus (GH) was significantly wider at the enrollment visit in the vaginal birth group (3.06 versus 2.22 cm, $p=0.001$). In the vaginal birth group, 82 women had a history of at least one forceps birth.

Figure 1 depicts the observed rate of change at points Ba, C and Bp for women who had at least 3 examinations (1091 of 1224, 89%). As noted, some women showed improvement in support over time (a negative slope, represented by the grey bars) but the majority demonstrated worsening (a positive slope, represented by the black bars). Estimates of the median rate of change (described in figure 1, with the interquartile range for each estimate) were compared at each point between the cesarean and vaginal birth groups. These comparisons were carried out using the weighted average procedures described in the methods section. The median rate of change in the anterior vaginal wall (Ba) was similar for the cesarean and vaginal delivery groups ($p=0.446$). However, the rate of change was significantly greater in the vaginal delivery group for both point C ($p<0.001$) and point Bp ($p<0.001$).

To further explore changes over time and using mixed effects models (see methods section), at each point (Ba, C and Bp) we estimated the mean value 5 years from first delivery (i.e., $\alpha_0 + \alpha_1 Z_{ij}$) as well as the mean change in support thereafter (i.e., $\beta_0 + \beta_1 Z_{ij}$), according to covariates. In univariable (unadjusted) models, parity and race had very little association with pelvic organ support. Parity (classified into three groups: 1, 2, and 3 deliveries) had no significant association with either support 5 years from first delivery or the rate of change for any of these three POPQ points. Because 95% of participants were of either Black or White race (Table 1), we classified race as Black versus all other races. Black race had a statistically marginal effect on the mean position of points Ba and Bp, with Black women having somewhat better support than women of other races. Specifically, among Black

women, the position of point Ba 5 years from first birth was -1.81 cm versus -1.66 cm for non-Black women ($p=0.048$) and the position of Bp was -2.42 cm versus -2.32 cm for non-Black women ($p=0.042$). There was no association between race and the rate of change in these points.

Univariable analyses for other covariates are shown in Table 2. Vaginal birth was associated with significantly worse support 5 years from first delivery at all three points (point Ba -1.32 versus -2.03 , $p<0.001$; point C -6.52 versus -6.73 , $p=0.003$; and point Bp -2.12 versus -2.54 , $p<0.001$). Vaginal birth was also associated with a significantly faster rate of progression for point C (0.76 cm versus 0.50 cm per 5-year interval, $p<0.001$) and for point Bp (0.32 cm versus 0.21 cm per 5-year interval, $p<0.001$) but not for point Ba (0.43 cm versus 0.49 cm per 5-year interval, $p=0.109$). Thus, vaginal birth was associated with worse support 5 years from first delivery at all three points and was associated with more rapid deterioration in support at the apex and posterior vaginal wall.

Also of note (Table 2) was the association between GH and support at all three points. A wider GH was associated with a lower position, 5 years from first delivery, for points Ba and Bp. There was also a strong and significant association between a wider GH and a faster rate of progression at all points. For example, at point C, the rate of change per 5-year interval was 0.49 cm among women with a GH < 2 cm, while the rate increased to 0.68 cm for those with a GH of 2.5 or 3 cm ($p<0.001$), and further increased to 0.72 cm for women with a GH of ≥ 3.5 cm ($p<0.001$).

Other variables with a significant association with support included the position of the apex (for Ba and Bp), maternal age at first delivery, and BMI. Position of the apex (point C) was significantly associated with support at points Ba and Bp 5 years from first delivery: poorer support at the apex was associated with poorer support at both the anterior and posterior vaginal wall. Support 5 years from first delivery was also associated with older age at delivery, with older women having poorer support at all points. Finally, BMI had paradoxical effects on Bp support: 5 years from first delivery the support was slightly worse among those with BMI ≥ 30 kg/m², but the subsequent rate of descent was slower in this group of obese women. Also, heavier women appeared to have better support at the apex 5 years from first delivery but no impact on the rate of change thereafter.

In multivariable analysis (Table 3), the impact of vaginal birth on vaginal support 5 years from first delivery was found to be attenuated by controlling for GH. For example, the difference in support at point Ba between the vaginal birth and cesarean birth groups was 0.71 cm in the unadjusted model (-1.32 versus -2.03), but this difference was only 0.41 cm in the adjusted model (-1.99 versus -2.40). Thus, GH accounted for some of the difference in support between the vaginal and cesarean groups. In addition, the association between vaginal birth and the rate of change in support after 5 years from first delivery was either attenuated (point C), rendered statistically insignificant (point Bp) or suggested a slower increase for the vaginal group (point Ba) by controlling for GH. In multivariable analysis, the association between vaginal birth and rate of change over time remained strongest for support at the apex (point C): even after controlling for GH, the rate of change at point C

was 0.42 cm per 5-year interval for those with cesarean births only and 0.61 cm for women with at least one vaginal birth.

Finally, a regression term for forceps delivery was added to the multivariable models. We found no association between history of forceps birth and the mean positions of the vaginal wall or apex 5 years from first birth. Likewise, we observed no statistically significant association between forceps delivery and the rate of change for all three points. For example, for Bp, the rate of change was 0.30 cm per 5 years in the forceps group versus 0.22 cm in the non-forceps group ($p = 0.108$).

Comment

This paper presents important data from a longitudinal study of pelvic organ support over time, including estimates of the rates of change over time in support of the anterior vaginal wall, the apex, and the posterior vaginal wall. Prior longitudinal studies of pelvic organ support have been quite limited, due in part to the expense and other burdens associated with multiple study visits for gynecologic (pelvic organ prolapse) examinations. A prior longitudinal study³ included 259 women followed for 559 woman-years. In that study, the authors defined “change in prolapse” as any difference in maximal vaginal descent by 1 cm or greater. In the present study, the larger sample (1224 women followed for 7055 woman-years), provided sufficient data to model support over a continuum and to compare the impact of vaginal versus cesarean delivery.

One of the most important findings of this study pertains to the differences in vaginal support between women who have delivered by cesarean only versus those who have experienced vaginal delivery. Vaginal birth was associated with worse support 5 years from first delivery and was also associated with more rapid deterioration in support at the apex. In addition, vaginal birth was associated with a wider genital hiatus, which was itself associated with more rapid deterioration in support over time. Controlling for the width of the genital hiatus, the independent association between vaginal birth and pelvic organ support was reduced in multivariable models. This finding is consistent with our prior work in this cohort⁶, which suggested that GH ≥ 2 cm at the time of study enrollment was associated with worsening support 12–18 months after study enrollment. This finding is also consistent with a prior cross-sectional study of women seeking care for pelvic floor disorders⁷, in which a wider genital hiatus was seen in women with poor apical support. Thus, the size of GH may account for some of the apparent association between vaginal birth and pelvic organ support. The genital hiatus was notably larger among those with a vaginal delivery and may be an independent marker for those at highest risk of prolapse progression.

In this analysis, forceps delivery was not significantly associated with changes over time in pelvic organ support. Our prior research⁸ suggested that forceps delivery was significantly associated with prolapse to or beyond the hymen at the time women presented for enrollment in this cohort study. However, in this analysis of longitudinal data, the observed associations between forceps delivery and rates of change in support of the anterior and posterior vaginal walls were not statistically significant. Nevertheless, the more rapid worsening of support among those delivered by forceps was in the direction expected. We

suspect that the small number of women exposed to forceps birth (82 of 1224 study participants) limited our power to make any definitive conclusions about the impact of forceps birth on the course and progression of pelvic organ prolapse.

Indeed one of the limitations of this study is the statistical power to investigate some associations. Despite a large study population, our sample is not sufficient to investigate all relevant factors. Moreover, the duration of follow up, while unprecedented, cannot allow us to extrapolate our findings across a lifespan.

A strength of this study is the annual assessment of prolapse with an objective and quantitative examination. Reviewers were masked to the participants' obstetrical histories, symptoms and prior examinations, limiting the potential for bias. Also, participants were not selected from a clinical (care-seeking) population, resulting in a study population more likely to be generalizable to a community sample of parous women.

This observational study provides valuable insights regarding the natural history of pelvic organ support. These data can serve as a foundation for the design of clinical trials and may also be valuable to clinicians counselling asymptomatic patients regarding the estimated progression of prolapse over time. For example, given that the median rate of change at point Ba was approximately half of a centimeter over 5 years (figure 1), an asymptomatic woman with anterior vaginal descent can be counselled that progression by 1 cm is likely to take between 9–10 years. Finally, these results suggest that the size of the genital hiatus may be an important marker for women at greatest risk for progression of prolapse. However, it does not necessarily follow that procedures to reduce the size of genital hiatus will retard the progression to prolapse, as the size of the genital hiatus may have a good predictive power but be a poor surrogate marker.⁹ Further research in this cohort will investigate whether the association between the size of the genital hiatus and prolapse progression may be mediated by levator ani structure and function, possibly providing novel targets for prevention intervention.

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Figure 1.

Distribution, among women with at least three study visits ($n=1091$), of the rates of change (per 5 year interval) in the position of each Pelvic Organ Prolapse Quantification point. Rates of change are shown for points Ba, C and Bp. Panels in the top row represent women with a history of only cesarean birth; panels in the lower row represent those with at least one vaginal birth. The grey bars indicate a rate of change less than zero (e.g., improvement in support). Shown in the bottom right corner of each panel is the percentage of women for whom the slope was positive (e.g., worsening in support), indicated by the black bars. Shown in the right upper corner of each panel is the median rate of change and the interquartile range.

Table 1

Characteristics of the study population at the first study visit (i.e., study entry).

	Cesarean only (n= 617)	At least one vaginal birth (n= 607)
Age at 1 st delivery (years)		
< 30	37% (230)	38% (231)
30 to < 35	35% (212)	36% (216)
35	28% (175)	26% (160)
Primary race		
White	77% (477)	84% (508)
Black	17% (106)	12% (72)
Asian	2% (13)	3% (18)
Other	4% (21)	1% (9)
No. deliveries at study entry		
1	31% (194)	24% (144)
2	55% (338)	58% (355)
3	14% (85)	18% (108)
Years from 1 st delivery at study entry	7.1 ± 1.7	6.9 ± 1.7
Body mass index at study entry (kg/m ²)		
< 25 kg/m ²	41% (256)	53% (325)
25 to < 30 kg/m ²	27% (165)	30% (181)
30 kg/m ²	32% (196)	17% (101)
Genital hiatus (GH) at study entry (cm)		
2 cm	54% (335)	19% (117)
2.5 to 3 cm	40% (248)	42% (257)
3.5 cm	6% (34)	39% (233)
No. of follow-up visits		
2 to 3	19% (116)	19% (116)
4 to 5	19% (117)	25% (154)
6 to 7	33% (204)	33% (201)
8 to 9	29% (180)	23% (136)
Longitudinal follow-up (years)	5.3 ± 2.1	5.0 ± 2.0
Person-visits	3659	3396

Values represent mean ± standard deviation or percentage (n).

Table 2

Mixed univariable (unadjusted) regression models for estimation of the mean value of each POPQ point (Ba, C and Bp), 5 years from first delivery, and for the mean change in position, per each subsequent 5 year interval (n=7055 woman-visits).

	Ba		C		Bp	
Covariate	Mean value (p-value)	Mean change (p-value)	Mean value (p-value)	Mean change (p-value)	Mean value (p-value)	Mean change (p-value)
Vaginal birth						
No	-2.03 (ref)	0.49 (ref)	-6.73 (ref)	0.50 (ref)	-2.54 (ref)	0.21 (ref)
Yes	-1.32 (<0.001)	0.43 (NS)	-6.52 (0.003)	0.76 (<0.001)	-2.12 (<0.001)	0.32 (<0.001)
Genital hiatus (GH)						
2 cm	-2.05 (ref)	0.41 (ref)	-6.51 (ref)	0.49 (ref)	-2.54 (ref)	0.20 (ref)
2.5 to 3 cm	-1.72 (<0.001)	0.52 (0.001)	-6.74 (<0.001)	0.68 (<0.001)	-2.36 (<0.001)	0.29 (<0.001)
3.5 cm	-1.20 (<0.001)	0.47 (NS)	-6.61 (NS)	0.72 (<0.001)	-2.07 (<0.001)	0.34 (<0.001)
Vaginal apex (C)						
-7 cm	-1.86 (ref)	0.38 (ref)			-2.45 (ref)	0.25 (ref)
-6.5 to -5.5 cm	-1.57 (<0.001)	0.38 (NS)	(NA)	(NA)	-2.28 (<0.001)	0.20 (NS)
-5 cm	-1.31 (<0.001)	0.34 (NS)			-2.08 (<0.001)	0.17 (0.013)
Age at 1 st delivery						
< 30 years	-1.73 (ref)	0.50 (ref)	-6.75 (ref)	0.68 (ref)	-2.43 (ref)	0.29 (ref)
30 to < 35 years	-1.69 (NS)	0.50 (NS)	-6.63 (NS)	0.65 (NS)	-2.29 (0.002)	0.27 (NS)
35 years	-1.62 (NS)	0.38 (0.009)	-6.44 (0.001)	0.52 (0.035)	-2.26 (0.001)	0.22 (NS)
Body mass index						
< 25 kg/m ²	-1.70 (ref)	0.46 (ref)	-6.52 (ref)	0.57 (ref)	-2.37 (ref)	0.30 (ref)
25 to < 30 kg/m ²	-1.65 (NS)	0.45 (NS)	-6.69 (0.014)	0.66 (NS)	-2.33 (NS)	0.26 (NS)
30 kg/m ²	-1.68 (NS)	0.49 (NS)	-6.74 (0.005)	0.69 (NS)	-2.27 (0.023)	0.21 (0.014)

Ref= reference; NS=not statistically significant; NA= not applicable

Table 3

Mixed multivariable (adjusted) regression models for estimation of the mean value of each POPQ point (Ba, C and Bp), 5 years from first delivery, and for the mean change in position, per each subsequent 5 year interval (n=7055 woman-visits). Each model includes covariates remaining statistically significant in the multivariable model.

Covariate	Ba		C		Bp	
	Mean value (p-value)	Mean change (p-value)	Mean value (p-value)	Mean change (p-value)	Mean value (p-value)	Mean change (p-value)
Vaginal birth						
No	-2.40 (ref)	0.38 (ref)	-6.71 (ref)	0.42 (ref)	-2.90 (ref)	(not included)
Yes	-1.99 (<0.001)	0.24 (<0.001)	-6.45 (0.001)	0.61 (0.003)	-2.62 (<0.001)	
Genital hiatus (GH)						
2 cm	-2.40 (ref)	0.38 (ref)	-6.71 (ref)	0.42 (ref)	-2.90 (ref)	0.23 (ref)
2.5 to 3 cm	-2.06 (<0.001)	0.47 (0.004)	-6.96 (<0.001)	0.58 (0.001)	-2.73 (<0.001)	0.31 (0.001)
3.5 cm	-1.65 (<0.001)	0.47 (0.033)	-6.85 (NS)	0.61 (0.003)	-2.51 (<0.001)	0.39 (<0.001)
Vaginal apex (C)						
-7 cm	-2.40 (ref)	(not included)	(NA)	(NA)	-2.90 (ref)	0.23 (ref)
-6.5 to -5.5 cm	-2.11 (<0.001)				-2.73 (<0.001)	0.18 (NS)
-5 cm	-1.88 (<0.001)				-2.54 (<0.001)	0.16 (0.011)
Age at 1st delivery						
< 30 years	(not included)	(not included)	-6.71 (ref)	(not included)	-2.90 (ref)	(not included)
30 to < 35 years			-6.61 (NS)		-2.79 (<0.001)	
35 years			-6.50 (0.003)		-2.78 (0.001)	
Body mass index						
< 25 kg/m ²	(not included)	(not included)	(not included)	(not included)	-2.90 (ref)	0.23 (ref)
25 to < 30 kg/m ²					-2.84 (NS)	0.17 (0.039)
30 kg/m ²					-2.78 (<0.001)	0.11 (<0.001)

Ref= reference; NS=not statistically significant; NA= not applicable; not included=some variables were not included in the multivariable models due to lack of significant association in univariable models