

GYNECOLOGY

Prolapse phenotypes and 12-month postoperative prolapse recurrence after apical native tissue surgery: a combined analysis using multicenter randomized trials and registry data



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BACKGROUND: Recurrence after pelvic organ prolapse surgery is not uncommon, and recurrence rates differ based on baseline prolapse characteristics, such as genital hiatus size and prolapse stage. Better understanding the relationship between anatomic prolapse subgroups and surgical outcomes may allow surgeons to individualize treatment decisions and improve outcomes. Clinically relevant prolapse phenotypes (subgroups) defined using the Pelvic Organ Prolapse Quantification system were previously identified. Therefore, study associations between these phenotypes and surgical outcomes in a large, prospectively collected dataset are sought.

OBJECTIVE: The primary aim of this study was to determine the association between a novel system of phenotyping prolapse and prolapse symptom recurrence 12 months postoperatively in women who underwent vaginal native-tissue apical prolapse surgery. Different prolapse phenotypes that would have different risks of prolapse recurrence were hypothesized. The secondary aims of the study were to determine the associations between the phenotypes and anatomic prolapse recurrence and new-onset stress urinary incontinence.

STUDY DESIGN: This was a secondary analysis of data combined from 3 multicenter randomized trials and 1 prospective, multicenter patient registry. Participants from these studies who underwent uterosacral ligament suspension or sacrospinous ligament fixation without mesh and had 12-month follow-up data were included and categorized into 1 of 8 phenotypes based on the Pelvic Organ Prolapse Quantification system: (1) no prolapse ($n=5$, excluded), (2) isolated anterior, (3) isolated posterior, (4) isolated apical, (5) anterior and posterior, (6) anterior-predominant and apical, (7) posterior-predominant and apical, and (8) anterior and posterior and apical. The primary outcome was symptomatic recurrence 12 months after surgery, which was defined as a positive response to the Pelvic Floor Distress Inventory “bulge” question with at least “somewhat” bother.

Univariate and multivariate logistic regression analyses (adjusted for prolapse stage [stage II vs stage III/IV] and previous hysterectomy) were developed for each outcome.

RESULTS: Of 704 participants, most (473 [67.2%]) had anterior-predominant and apical prolapse (used as the reference group), followed by the anterior and posterior and apical (101 [14.3%]) and isolated apical (45 [6.4%]) phenotypes. Overall, 184 patients (26.1%) had sacrospinous ligament fixation, 520 patients (73.9%) had uterosacral ligament suspension, and 454 patients (64.5%) had midurethral slings. Overall, symptomatic prolapse recurrence occurred in 65 patients (9.2%), ranging from 0.0% to 29.0% across phenotype groups, and was particularly uncommon in the isolated posterior (0.0%) and isolated apical (2.2%: 1 participant) phenotypes. However, the phenotype group was not significantly associated with symptomatic recurrence in univariate or multivariate analysis. Hispanic ethnicity (odds ratio, 2.25 [95% confidence interval, 1.17–4.35]; $P=.015$), private insurance (odds ratio, 0.58 [95% confidence interval, 0.35–0.98]; $P=.042$), and vaginal parity (odds ratio, 1.19 [95% confidence interval, 1.02–1.40]; $P=.030$) were significantly associated with recurrence. Similarly, the phenotype was not significantly associated with anatomic recurrence or new or worsening stress urinary incontinence.

CONCLUSION: Prolapse Pelvic Organ Prolapse Quantification phenotypes were not associated with symptomatic recurrence after native tissue repair surgery. Most women who underwent native tissue apical prolapse surgery have anterior-predominant and apical prolapse. Larger studies may be needed to identify differences in outcomes among less common phenotype groups.

Key words: Pelvic Organ Prolapse Quantification, phenotype, prolapse, prolapse surgery, surgery

Introduction

Pelvic organ prolapse (POP) is common and becoming more prevalent, with an estimated increase in prevalence in American women from 3.3 million in

2010 to 4.9 million in 2050.¹ Since 1996, the Pelvic Organ Prolapse Quantification (POP-Q) system has been the de facto standard for measuring, reporting, and communicating about POP in published research.² The POP-Q system, composed of 9 quantitative measurements and an ordinal staging system, has good intra- and interobserver reliability.^{2,3} Moreover, there are significant limitations to the POP-Q ordinal staging system,⁴ which does not account for the various

configurations or clinical phenotypes in which prolapse presents. For example, a patient with anterior vaginal wall and apical prolapse just beyond the hymen with normal posterior wall support would have the same stage (stage II) as a patient with normal anterior wall and apical support but with posterior wall prolapse just beyond the hymen. Although these 2 patients have the same prolapse stage, the underlying pathophysiology, symptomatology, best

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AJOG at a Glance

Why was this study conducted?

Prolapse surgery outcomes might be improved with more personalized treatment decisions based on baseline patient factors. This study tested whether previously defined prolapse phenotypes defined using the Pelvic Organ Prolapse Quantification (POP-Q) examination were associated with outcomes after vaginal native-tissue prolapse surgery.

Key findings

Prolapse phenotype was not associated with symptomatic recurrence, although recurrence seemed rare in the less common isolated posterior (0.0%) and isolated apical (2.2%; 1 participant) phenotype groups. Most women who underwent vaginal native-tissue apical prolapse surgery had anterior-predominant and apical prolapse.

What does this add to what is known?

Our results contribute to a growing body of research focused on better understanding how baseline parameters (beyond the POP-Q stage) may affect surgical results.

treatment options, and recurrence risk between these 2 clinical phenotypes may be different.

The concept of identifying and reliably defining prolapse phenotypes or subgroups is important because different prolapse phenotypes may arise from different pathophysiological processes and, thus, respond differently to treatment. Thus, a better understanding of the potential relationships between the anatomic prolapse subgroups and surgical outcomes may allow surgeons to individualize treatment decisions and improve outcomes. Other authors have described prolapse phenotypes. Lamblin et al⁵ reviewed the anatomic support structures of the anterior vaginal wall and discussed various types of cystocele, including apical, midline, and lateral cystoceles. However, the method for identifying these phenotypes has been subjective and has been shown to lack accuracy.⁶

Lowder et al⁷ used unsupervised machine learning to identify potential prolapse phenotypes based on POP-Q findings and found some relationships between the phenotype group and sacrocolpopexy outcomes in patients with milder stage II prolapse but not in those with stage III/IV prolapse.

We recently proposed phenotypes of prolapse that can be readily defined

using existing POP-Q measurements.⁸ The system consists of 8 POP subtypes or “phenotypes” that are clinically meaningful and can be categorized using the existing POP-Q system. We hypothesized that different phenotypes of prolapse will have different risks of prolapse recurrence after surgery. The primary aim of this study was to determine the association between these phenotypes and prolapse symptom recurrence 12 months postoperatively in women undergoing either uterosacral ligament suspension (USLS) or sacrospinous ligament fixation (SSLF). The secondary aims of this study included determining the association between phenotypes and anatomic recurrence and new or worsened stress urinary incontinence (SUI). An additional secondary aim was to evaluate the association between other important demographic and medical characteristics, such as individual POP-Q values, with symptom recurrence, anatomic recurrence, and new or worsened SUI.

Materials and methods

The University of Iowa Institutional Review Board determined this study to be exempt, as all data used were deidentified. This was a secondary analysis of patients enrolled in 1 of 3 previous multicenter randomized trials evaluating vaginal

native-tissue apical prolapse surgery or 1 prospective, multicenter prolapse treatment registry. Patient data from 3 National Institutes of Health–funded randomized trials conducted by the Pelvic Floor Disorders Network, including the Operations and Pelvic Muscle Training in the Management of Apical Support Loss (OPTIMAL), Outcomes Following Vaginal Prolapse Repair and Midurethral Sling (OPUS), and Study of Uterine Prolapse Procedures Randomized (SUPeR) trials, were eligible for inclusion.^{9–11} Patients who underwent USLS or SSLF without mesh and had complete 12-month follow-up data available were included. Patients enrolled in the American Urogynecologic Society Pelvic Floor Disorders Registry – Research (PFDR-R) with the same criteria were also included.¹² Table 1 presents the study design, inclusion criteria, study intervention, and follow-up information for each original study. Data obtained from each original study included baseline demographics, elements of medical and surgical history, baseline and 12-month follow-up Pelvic Floor Distress Inventory (PFDI) information, baseline POP-Q data, and surgical procedures performed. In addition to the raw POP-Q data, the maximal vaginal descent (MVD) was calculated for each patient. This was defined as the greatest of the POP-Q points, Ba, C, or Bp.

Data from all patients meeting the inclusion criteria were compiled into a single database and categorized into 1 of 8 phenotypes based on the baseline POP-Q (Table 2).⁸ Of note, 2 guiding principles were used to define the phenotypes. First, we assert that prolapse exists when either the anterior and/or posterior vaginal wall descends to at least the hymen or the apex (cervix or cuff) descends to at least half of the total vaginal length (TVL). Second, we considered prolapse as existing in 1 of 3 vaginal compartments or combinations of the 3 vaginal compartments (anterior wall, posterior wall, and apex). Using these principles, there are 3 phenotypes representing prolapse limited to a single compartment: isolated anterior wall (A), isolated posterior wall (P), and isolated

TABLE 1

Description of randomized trials and research registry whose participants were considered for inclusion in this combined secondary data analysis

Primary study and n (%) included in current study	Study design	Number of sites	Study inclusion criteria	Study interventions	Follow-up POP-Q
Operations and Pelvic Muscle Training in the Management of Apical Support Loss (OPTIMAL) Trial (261 [37.1%])	2 × 2 factorial RCT comparing SSLF and USLS and the effect of perioperative pelvic floor muscle training; primary outcomes were prolapse at 24 mo and urinary symptoms at 6 mo.	9	Women aged ≥18 y, stage II–IV prolapse with bulge symptoms, apical prolapse at least half TVL, objective SUI.	SSLF was unilateral modification of Michigan 4-wall technique; USLS was bilateral medication of Shull technique; both procedures used 2 absorbable and 2 permanent sutures; all patients with a uterus underwent vaginal hysterectomy; all patients received retropubic MUS; patients also randomized to usual perioperative care or an individualized pelvic floor muscle training program.	Masked research personnel
Outcomes Following Vaginal Prolapse Repair and Midurethral Sling (OPUS) Trial (230 [32.7%])	RCT comparing MUS to sham MUS incisions; primary outcomes were urinary incontinence at 3 and 12 mo.	7	Women who underwent vaginal prolapse surgery for stage II to IV prolapse with no SUI symptoms; exclusions were previous MUS, receiving SUI treatment, contraindications to MUS or planned pregnancy with 12 mo.	Patients were randomized to retropubic MUS or sham MUS incisions; any vaginal prolapse surgery could be performed; most patients underwent native-tissue USLS or SSLF; the only restriction on surgical technique was Kelly plication sutures were disallowed.	Nonmasked research personnel
Study of Uterine Prolapse Procedures Randomized (SUPeR) Trial [82 [11.6%])	RCT comparing transvaginal mesh hysteropexy to vaginal hysterectomy and USLS; primary outcome was treatment failure at least 36 mo.	9	Women aged ≥21 y, prolapse beyond hymen and apical prolapse at least half TVL, amenorrheic at least 1 y and completed child bearing; those with previous apical prolapse surgery; mesh prolapse surgery or uterine abnormalities were excluded.	Randomization was to a transvaginal polypropylene mesh hysteropexy kit or USLS performed with one absorbable and one permanent suture on each side; concomitant anterior/posterior repairs and full-length MUS were allowed.	Clinician other than the surgeon
American Urogynecologic Society (AUGS) Pelvic Floor Disorders Registry — Research (PFDR-R) (131 [18.6%])	Voluntary multicenter, real-world registry of patients who underwent prolapse treatment with pessary or surgery with up to the 36-mo follow-up.	11	Adult women electing prolapse treatment with surgery or pessary; exclusions were pregnancy or inability to participate.	The type of pessary or surgery was entirely at the discretion of the patient and surgeon; there were also no restrictions on USLS technique.	Per usual clinical care

Participants who underwent uterosacral ligament suspension or sacrospinous ligament fixation without mesh and had complete 12-month follow-up data from these studies were included.

MUS, midurethral sling; POP-Q, Pelvic Organ Prolapse Quantification; RCT, randomized controlled trial; SSLF, sacrospinous ligament fixation; USLS, uterosacral ligament suspension; TVL, total vaginal length; SUI, stress urinary incontinence.

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TABLE 2

Prolapse phenotypes

Phenotype	Description	POP-Q Criteria		
		Ba	C	Bp
0	No prolapse	<0	<TVL/2	<0
A	Isolated anterior	³ 0	<TVL/2	<0
P	Isolated posterior	<0	<TVL/2	³ 0
C	Isolated apical	Aa<0 and (Ba<0 or =C)	³ TVL/2	Ap<0 and (Bp<0 or ≤C)
AP	Anterior and posterior	³ 0	<TVL/2	³ 0
AC	Anterior-predominant and apical	³ 0 and >Bp	³ TVL/2	
PC	Posterior-predominant and apical		³ TVL/2	³ 0 and >Ba
APC	Anterior and posterior and apical	³ 0 and =Bp	³ TVL/2	

POP-Q, Pelvic Organ Prolapse Quantification; TVL, total vaginal length.

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apical (C). There are 3 phenotypes representing prolapse of 2 compartments: anterior and posterior wall (AP), anterior-predominant and apical (AC), and posterior-predominant and apical (PC). There is 1 phenotype representing prolapse of all 3 compartments: anterior, posterior, and apical (APC). Lastly, we defined 1 phenotype as no prolapse (0) to account for individuals with relevant prolapse symptoms and lesser degrees of anatomic prolapse. Of note, 5 subjects with no prolapse were excluded from the analysis (1 from OPUS and 4 from PFDR-R). Table 2 outlines how each phenotype was defined using the POP-Q. Except for the isolated apical (C) phenotype, each phenotype is mutually exclusive. In some circumstances, the same set of POP-Q values could fulfill the criteria for both the isolated apical (C) phenotype and 1 of the phenotypes that include apical prolapse (AC, PC, or APC). For these circumstances, the isolated apical (C) phenotype was given priority and assigned.

The primary outcome was symptomatic prolapse recurrence, which was defined as any degree of bothersome vaginal bulge based on PFDI question 5, assessed at 12 months after surgery.¹³ Anatomic recurrence was defined as any prolapse beyond the hymen. New or worsened SUI was based on any negative (ie, more symptomatic) change in

response to PFDI question 20. For example, a subject would be considered to meet the criteria for this outcome if they reported no SUI at baseline and SUI at follow-up. In addition, a subject would meet the criteria if they reported SUI at baseline and SUI with a greater degree of bother at follow-up.

Demographics, medical history, and surgical details were compared between the groups using Kruskal-Wallis rank-sum tests and Fisher exact tests. Univariate logistic regression mixed models were used to examine each independent variable and each outcome with a random intercept to account for inherent variability between different studies. In addition, multivariate logistic regression mixed models were constructed. A series of models were fit in which each independent variable was examined for each outcome while controlling for POP-Q severity (stage II vs stage III/IV) and previous hysterectomy status. We adjusted for these variables because they differed across phenotype groups, and we hypothesized before data analysis that they may be associated with outcomes. In addition, a random intercept was used in each study in the multivariate models. The anterior-predominant and apical (AC) phenotype was the most common phenotype and served as the reference group for comparisons between the phenotypes.

In addition, Cochran-Mantel-Haenszel tests were performed to determine whether there was an association between the phenotypes and primary outcome when the population was stratified by POP-Q severity (stage II vs stage III/IV), hysterectomy status (yes/no), and genital hiatus (GH; ³4 or <4 cm). Cochran-Mantel-Haenszel tests were used to maximize our power, given the small sample size of certain phenotypes in our study. We considered that our results may have been affected by the inclusion of a nonrandomized patient registry where the patient and surgeon made the decisions for the type of prolapse surgery. Therefore, we planned a sensitivity analysis that excluded the participants from the registry.

The sample size was determined by the available patient population in the included studies. Statistical significance was defined as *P*<.05. Statistical analyses were performed using R (version 4.5.1; R Foundation for Statistical Computing, Vienna, Austria).

Results

A total of 704 patients were included: 261 (37.1%) from OPTIMAL, 230 (32.7%) from OPUS, 82 (11.6%) from SUPeR, and 131 (18.6%) from PFDR-R (Table 1). Of the 704 patients, most were in the AC (473 [67.1%]), APC (101 [14.3%]), and C (45 [6.4%]) phenotypes

(Table 3). The mean age significantly varied by phenotype from 57 years (SD, 11.2) in the AP phenotype to 69 years (SD, 9.2) in the PC phenotype ($P<.001$). In addition, the frequency of previous hysterectomy significantly varied by phenotype, ranging from 5 (11%) in the C phenotype to 7 (78%) in the P phenotype. Overall, 184 patients (26.1%) had SSLF, 520 patients (73.9%) had USLS, and 454 patients (64.5%) had midurethral slings (MUSs).

Across the total population, 65 patients (9.2%) had symptomatic prolapse recurrence, and 100 patients (14.2%) had anatomic recurrence. The rates of symptomatic and anatomic prolapse recurrences by prolapse phenotype groups are presented in Table 4. Symptomatic recurrence varied across phenotype groups, ranging from a low of 0% in the P phenotype to a high of 29% in the AP phenotype. Although the symptomatic recurrence rates seemed to differ across the phenotype groups and were particularly low in the P phenotype (0.0%) and C phenotype (2.2%: 1 participant), the phenotype group was not significantly associated with symptomatic recurrence in the unadjusted (Supplemental Table) or adjusted (Table 5) logistic regression models. For modeled relationships with the primary outcome (bulge symptom), Hispanic ethnicity (odds ratio [OR], 2.25 [95% confidence interval (CI), 1.17–4.35]; $P=.015$), private insurance (OR, 0.58 [95% CI, 0.35–0.98]; $P=.042$), and vaginal parity (OR, 1.19 [95% CI, 1.02–1.40]; $P=.030$) were significantly associated with recurrence (Table 5). The Cochran-Mantel-Haenszel tests did not find significant evidence that the odds of symptomatic recurrence for any phenotype relative to phenotype AC were different than 1. This was the case both when examined overall and when stratified by POP-Q severity, previous hysterectomy, or GH of ≥ 4.0 . The results from the sensitivity analysis (limited to participants from the randomized trials) were overall consistent with the primary findings (data not shown).

Anatomic recurrence rates varied from 0% to 19% across the phenotype groups

(Table 4). Similar to the symptomatic recurrence results, the phenotype was not associated with anatomic recurrence (Table 5). Several baseline predictors were associated with anatomic recurrence in the adjusted analysis, including Hispanic ethnicity (OR, 1.92 [95% CI, 1.06–3.46]; $P=.031$), private insurance (OR, 0.55 [95% CI, 0.35–0.85]; $P=.004$), and vaginal parity (OR, 1.24 [95% CI, 1.08–1.42]; $P>.001$). In addition, multiple baseline individual POP-Q measurements were significantly associated with anatomic recurrence, including GH (OR, 1.31 [95% CI, 1.11–1.56]; $P=.002$), Aa (OR, 1.20 [95% CI, 1.01–1.44]; $P=.038$), Ba (OR, 1.27 [95% CI, 1.14–1.41]; $P<.001$), C (OR, 1.11 [95% CI, 1.04–1.18]; $P<.001$), D (OR, 1.09 [95% CI, 1.02–1.17]; $P=.008$), and MVD (OR, 1.26 [95% CI, 1.13–1.42]; $P<.001$).

In addition, new or worsening SUI results are presented in Tables 4 and 5. Phenotype A was significantly associated with new or worsening SUI (OR, 8.13 [95% CI, 2.77–23.8]; $P<.001$) in the multivariate model (Table 5). Moreover, this outcome was associated with baseline SUI symptoms (OR, 0.12 [95% CI, 0.04–0.36]; $P<.001$) and concurrent MUS (OR, 0.10 [95% CI, 0.05–0.24]; $P<.001$).

Comment

Principal findings

In this study of more than 700 patients who underwent apical native-tissue vaginal prolapse surgery, baseline anatomic prolapse phenotypes were not associated with 12-month symptomatic prolapse recurrence. However, no patient with phenotype P had symptomatic or anatomic recurrence. Similarly, only 1 patient with phenotype C had a symptomatic recurrence, and 2 patients had an anatomic recurrence. The smaller sample sizes in these less common phenotypes may have limited our ability to identify potentially meaningful differences in our outcomes.

Results in the context of what is known

Lowder et al⁷ aimed to develop a clinical prediction model that uses preoperative scores on the POP-Q examination to

predict outcomes after minimally invasive sacrocolpopexy. In contrast to our a priori defined phenotypes, they used machine learning to identify phenotype clusters predictive of surgical success. Their phenotypes bear some resemblance to ours. However, they do not offer a method of clearly categorizing any given patient into a phenotype with POP-Q values. In contrast to our findings, they found their phenotypes associated with surgical success in patients with stages II to IV uterovaginal prolapse and stage II posthysterectomy prolapse but not stage III/IV posthysterectomy prolapse. Their definition of success was less than stage II prolapse, which is a less clinically relevant definition of success than subjective recurrence based on bulge symptoms or prolapse beyond the hymen.¹⁴ Thus, our results may differ from theirs because we used a different definition of surgical success and examined vaginal native-tissue surgery as opposed to sacrocolpopexy.

Some research suggests that enlarged GH may be associated with prolapse recurrence. In addition, enlarged GH may represent a phenotype (likely identifying those with specific levator injury) that is associated with recurrence. Bradley et al¹⁵ examined the subjects from the SUPeR trial who had vaginal native tissue surgery (one of the populations also included in the current study). They categorized patients into those with persistently enlarged GH, improved GH, or stably normal GH. Patients with a persistently enlarged GH had a higher risk of prolapse recurrence. However, this finding became nonsignificant when adjusted for advanced prolapse at baseline. This result is concordant with our findings. Increased GH measured continuously was associated with anatomic recurrence on univariate and multivariate analyses. GH measured dichotomously (≥ 4 or <4 cm) was significant in the univariate analysis but became nonsignificant ($P=.076$) with recurrence on multivariate analysis when including baseline prolapse severity.

In other predictors of prolapse surgery outcomes, we found that women of Hispanic ethnicity were at increased risk

TABLE 3

Baseline characteristics presented by prolapse phenotype groups, determined using the POP-Q

Variable	Overall	A	P	C	AP	AC	PC	APC	P value
n	704 (100.0)	31 (4.4)	9 (1.3)	45 (6.4)	7 (1.0)	473 (67.2)	38 (5.4)	101 (14.3)	
Age (y), mean (SD)	61.3 (9.9)	61 (9.6)	65 (7.8)	64 (8.8)	57 (11.2)	61 (9.6)	69 (9.2)	64 (10.6)	<.001
BMI (kg/m ²), mean (SD)	28.2 (5.1)	27.2 (4.2)	26.1 (2.9)	27.4 (5.9)	30.9 (6.5)	28.1 (4.9)	29.9 (5.3)	28.9 (5.9)	.091
Hispanic ethnicity	87 (12.0)	1 (3.0)	0 (0)	3 (7.0)	0 (0)	74 (16.0)	1 (3.0)	9 (8.0)	.022
Race									.13
White	614 (87.0)	26 (84.0)	9 (100.0)	35 (78.0)	6 (86.0)	415 (88.0)	36 (95.0)	87 (86.0)	
Black	40 (5.7)	5 (16.0)	0 (0)	3 (7.0)	0 (0)	23 (5.0)	1 (3.0)	8 (8.0)	
Other	50 (7.1)	0 (0)	0 (0)	7 (16.0)	1 (14.0)	35 (7.0)	1 (3.0)	6 (6.0)	
Education									.15
Less than high school	72 (11.0)	2 (9.5)	0 (0)	1 (2.5)	0 (0)	61 (14.0)	2 (6.3)	6 (6.3)	
High school/GED	171 (27.0)	5 (24.0)	3 (43.0)	7 (18.0)	1 (17.0)	125 (28.0)	5 (16.0)	25 (26.0)	
Some college/associate	160 (25.0)	5 (24.0)	2 (29.0)	10 (25.0)	1 (17.0)	102 (23.0)	11 (34.0)	29 (31.0)	
4-y college degree	140 (22.0)	5 (24.0)	1 (14.0)	14 (35.0)	1 (17.0)	96 (22.0)	6 (19.0)	17 (18.0)	
Graduate/professional	99 (15.0)	4 (19.0)	1 (14.0)	8 (20.0)	3 (50.0)	57 (13.0)	8 (25.0)	18 (19.0)	
Private insurance	368 (52.0)	11 (35.0)	4 (44.0)	25 (56.0)	5 (71.0)	258 (55.0)	21 (55.0)	44 (44.0)	.20
Smoker	232 (34.0)	11 (37.0)	3 (38.0)	16 (37.0)	1 (14.0)	155 (33.0)	18 (47.0)	28 (28.0)	.40
Vaginal parity, median (IQR)	2 (2–3)	2 (1–3)	2 (2–3)	2 (2–3)	2 (2–2)	2 (2–3)	3 (2–4)	3 (2–3)	.20
Previous POP surgery	52 (7.4)	5 (16.0)	0 (0)	1 (2.2)	0 (0)	35 (7.4)	3 (7.9)	8 (7.9)	.50
Previous SUI surgery	22 (3.8)	0 (0)	0 (0)	0 (0)	1 (2.8)	13 (3.2)	4 (15.0)	4 (4.4)	.20
Previous hysterectomy	171 (24.0)	14 (45.0)	7 (78.0)	5 (11.0)	3 (43.0)	91 (19.0)	18 (47.0)	33 (33.0)	<.001
SUI symptoms	323 (47.0)	7 (25.0)	2 (25.0)	22 (52.0)	3 (50.0)	228 (49.0)	20 (56.0)	41 (42.0)	.10
Apical surgery performed									.031
Uterosacral ligament suspension	520 (74.0)	27 (87.0)	5 (56.0)	32 (71.0)	5 (71.0)	355 (75.0)	20 (53.0)	76 (75.0)	
Sacrospinous ligament fixation	184 (26.0)	4 (13.0)	4 (44.0)	13 (29.0)	2 (29.0)	118 (25.0)	18 (47.0)	25 (25.0)	
Concurrent MUS	454 (64.0)	14 (45.0)	2 (22.0)	31 (69.0)	4 (57.0)	316 (67.0)	22 (58.0)	65 (64.0)	.027
POP-Q stage									<.001
II	218 (31.0)	15 (48.0)	5 (56.0)	25 (56.0)	4 (57.0)	130 (27.0)	18 (47.0)	21 (21.0)	

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(continued)

TABLE 3

Baseline characteristics presented by prolapse phenotype groups, determined using the POP-Q (continued)

Variable	Overall	A	P	C	AP	AC	PC	APC	P value
III	438 (62.0)	16 (52.0)	4 (44.0)	19 (42.0)	3 (43.0)	324 (68.0)	19 (50.0)	53 (52.0)	
IV	48 (6.8)	0 (0)	0 (0)	1 (2.2)	0 (0)	19 (4.0)	1 (2.6)	27 (27.0)	
POP-Q GH	4.0 (4.0–5.0)	4.0 (3.0–4.0)	4.0 (3.5–4.5)	4.0 (3.5–5.0)	3.5 (3.0–5.0)	4.5 (4.0–5.0)	5.0 (4.0–6.0)	5.0 (4.0–6.0)	<.001
POP-Q GH									
≥4 cm	573 (81.0)	16 (52.0)	6 (67.0)	33 (73.0)	3 (43.0)	393 (83.0)	31 (82.0)	91 (90.0)	<.001
POP-Q TVL	9.0 (8.0–10.0)	8.0 (7.5–9.0)	9.0 (8.0–9.5)	9.0 (8.0–10.0)	9.0 (7.5–9.0)	9.0 (8.0–10.0)	9.0 (8.0–10.0)	9.0 (8.0–10.0)	.011
POP-Q Aa	1.0 (0.0–3.0)	1.0 (0.0–2.0)	–1.5 (–2.0 to –1.0)	–1.0 (–1.0 to –1.0)	1.0 (1.0–1.0)	2.0 (1.0–3.0)	–1.0 (–1.0 to 0.0)	2.0 (0.0–3.0)	<.001
POP-Q Ba	2.0 (1.0–3.5)	2.0 (0.0–2.0)	–2.0 (–2.0 to –1.0)	–1.0 (–1.0 to 2.0)	1.0 (1.0–2.0)	2.0 (1.0–3.0)	–0.5 (–1.0 to 0.0)	4.0 (2.0–6.0)	<.001
POP-Q C	–2.0 (–3.0 to 2.0)	–5.0 (–6.0 to –4.0)	–6.0 (–7.0 to 5.0)	1.0 (–2.0 to 3.0)	–6.0 (–6.0 to –5.0)	–2.0 (–3.0 to 1.0)	–3.0 (–4.0 to –2.0)	4.0 (1.0–6.0)	<.001
POP-Q D	–5.0 (–6.0 to –3.0)	–7.0 (–7.0 to –6.0)	–6.0 (–7.0 to –6.0)	–4.0 (–6.0 to –2.0)	–7.0 (–7.0 to –6.5)	–5.0 (–6.0 to –4.0)	–5.0 (–6.5 to –4.5)	–3.5 (–5.0 to 2.0)	<.001
POP-Q Ap	–1.0 (–2.0 to 0.0)	–2.0 (–2.0 to –1.0)	0.0 (0.0–1.5)	–2.0 (–2.0 to –1.5)	0.0 (0.0–0.5)	–2.0 (–2.0 to –1.0)	1.0 (1.0–2.0)	0.0 (–1.0 to –3.0)	<.001
POP-Q Bp	–1.0 (–2.0 to 0.5)	–2.0 (–2.0 to –1.0)	1.0 (0.0–2.0)	–2.0 (–2.0 to –0.5)	0.0 (0.0–0.5)	–1.0 (–2.0 to –0.5)	1.5 (1.0–3.0)	4.0 (2.0–6.0)	<.001

Data are presented as number (percentage) or median (interquartile range), unless otherwise stated.

A, isolated anterior; AC, anterior-predominant and apical; AP, anterior and posterior; APC, anterior and posterior and apical; C, isolated apical; GED, General Education Development; MUS, midurethral sling; P, isolated posterior; PC, posterior-predominant and apical; POP-Q, Pelvic Organ Prolapse Quantification; SD, standard deviation; TVL, total vaginal length.

Weston. Prolapse phenotypes and 12-month postoperative prolapse recurrence. *Am J Obstet Gynecol* 2026.

TABLE 4

Primary and secondary outcomes presented for each prolapse phenotype group

Variable	Overall	A	P	C	AP	AC	PC	APC
n	704 (100.0)	31 (4.4)	9 (1.3)	45 (6.4)	7 (1.0)	473 (67.2)	38 (5.4)	101 (14.3)
Symptomatic recurrence	65 (9.2)	3 (9.7)	0 (0)	1 (2.2)	2 (29.0)	43 (9.1)	4 (11.0)	12 (12.0)
Anatomic recurrence	100 (14.2)	4 (19.0)	0 (0)	2 (4.9)	1 (17.0)	70 (16.0)	5 (16.0)	18 (19.0)
New or worsening SUI	37 (5.3)	7 (26.0)	0 (0)	1 (2.4)	1 (17.0)	19 (4.1)	4 (11.0)	5 (5.1)

Data are presented as number (percentage).

A, isolated anterior; AC, anterior-predominant and apical; AP, anterior and posterior; APC, anterior and posterior and apical; C, isolated apical; P, isolated posterior; PC, posterior-predominant and apical; SUI, stress urinary incontinence.

Weston. Prolapse phenotypes and 12-month postoperative prolapse recurrence. *Am J Obstet Gynecol* 2026.

of symptomatic prolapse recurrence. Conversely, in the univariate model, women with private insurance were at decreased risk of symptomatic recurrence. In addition, other authors have demonstrated that prolapse surgery outcomes are associated with racial and socioeconomic factors. Rahn et al¹⁶ identified Latina ethnicity as a risk factor for recurrence after vaginal native-tissue prolapse surgery. Rozycki et al¹⁷ found that non-White patients with lower socioeconomic status had increased postoperative complications and fewer intraoperative complications from POP surgery and that White patients with higher socioeconomic status had more intraoperative complications. In addition, another secondary analysis of the OPTIMAL and E-OPTIMAL (extended) trial confirmed that Hispanic ethnicity was a risk factor for surgical failure up to 5 years postoperatively.¹⁸ Other research studies found that Hispanic and Native American women have a higher level of bother associated with stage II prolapse than non-Hispanic White women.¹⁹ Although varying outcomes have been reported in patients of varying race and ethnicity, these populations remain underrepresented in prolapse research, as confirmed by this study.

Clinical implications

This study demonstrates that major prolapse surgery trials primarily enroll women with phenotype AC prolapse. This phenotype accounted for 67.2% of the patients across these 3 trials and the PFDR-R who were included. This is not

surprising given that these trials are enrolling patients who underwent apical prolapse surgery. In our previous analysis of women scheduled for any prolapse surgery (not limited to USLS or SSLF) at our institution, 232 of 501 patients (46.1%) had phenotype AC.⁸ Less is known about the other phenotypes, and future research with larger populations should aim to clarify whether these less common phenotypes have a lower risk of prolapse recurrence. This could improve the counseling of patients by providing them with surgical recurrence rates based on their individual prolapse phenotype. Furthermore, this concept could eventually lead to a more nuanced and individualized approach to the selection of surgical procedures. For example, women with phenotype C prolapse may have a very low risk of recurrence with USLS or SSLF than those with the more common phenotype AC. Thus, selecting a sacrocolpopexy with mesh may differentially benefit women with phenotype AC more than those with phenotype C.

Research implications

Future research should focus on identifying clinically meaningful prolapse phenotypes that correspond to unique underlying pathophysiology, symptomatology, and treatment outcomes. Although this study focuses on phenotyping using the features of a clinical examination (POP-Q), other factors may further build on the idea of phenotyping. For example, certain genetic variations in relevant tissues may predispose to or protect against the

development of prolapse.²⁰ These advances will facilitate more individualized, patient-specific counseling. Clinical trials should seek to clarify the surgical outcomes for the less common prolapse phenotypes, and the authors should consider reporting outcomes separately for patients without anterior-predominant and apical prolapse.

Strengths and limitations

The strengths of this study include the use of data from rigorously performed, multicenter randomized trials and a multicenter POP treatment registry representing various geographic populations and surgeons across the United States. The other primary strength is the use of a novel, easy-to-use method for phenotyping prolapse based on the already widely used POP-Q system. The limitations of this study include underrepresentation of non-White women and a relatively short follow-up time of 12 months, which was limited by the OPUS trial, which had only a 12-month follow-up. Lastly, although we included data from 4 different multicenter studies, a larger study population may be needed to identify differences in outcomes across the less common prolapse phenotype groups.

Conclusion

In this combined trial and registry dataset analysis, baseline prolapse phenotypes based on the POP-Q were not associated with symptomatic and anatomic prolapse recurrence 12 months after native-tissue apical POP surgery. Although the phenotype group

TABLE 5

Associations between baseline patient characteristics and primary and secondary outcomes, adjusted for prolapse severity (POP-Q stage II vs stage III/IV) and previous hysterectomy and with a random intercept for the original study

Variable	Symptomatic recurrence	Anatomic recurrence	New or worsening SUI
Phenotype			
A	1.06 (0.31–3.70)	1.49 (0.46–4.81)	8.13 (2.77–23.8) ^a
P	Not estimable	Not estimable	Not estimable
C	0.23 (0.03–1.72)	0.35 (0.08–1.52)	0.67 (0.09–5.08)
AP	3.98 (0.74–21.5)	1.23 (0.13–11.5)	4.17 (0.44–3.53)
AC	—	—	—
PC	1.16 (0.39–3.51)	1.13 (0.40–3.16)	3.24 (0.99–10.6)
APC	1.34 (0.67–2.65)	1.07 (0.60–1.94)	1.27 (0.46–3.53)
POP-Q values			
POP-Q GH (continuous)	1.05 (0.85–1.30)	1.31 (1.11–1.56) ^a	1.19 (0.91–1.57)
POP-Q GH (dichotomous)			
<4 cm	—	—	—
≥4 cm	1.12 (0.56–2.24)	1.94 (0.93–4.04)	1.13 (0.47–2.73)
POP-Q TVL	1.04 (0.82–1.33)	0.89 (0.73–1.09)	1.00 (0.73–1.36)
POP-Q Aa	0.99 (0.82–1.21)	1.20 (1.01–1.44) ^a	1.09 (0.83–1.42)
POP-Q Ba	1.06 (0.93–1.22)	1.27 (1.14–1.41) ^a	1.06 (0.89–1.26)
POP-Q C	1.02 (0.95–1.10)	1.11 (1.04–1.18) ^a	0.95 (0.86–1.05)
POP-Q D	0.98 (0.88–1.08)	1.09 (1.02–1.17) ^a	0.91 (0.78–1.06)
POP-Q Ap	1.01 (0.85–1.19)	1.00 (0.87–1.15)	1.22 (1.00–1.50) ^b
POP-Q Bp	1.08 (0.98–1.18)	1.06 (0.98–1.14)	1.07 (0.95–1.21)
Maximal vaginal descent	1.04 (0.89–1.22)	1.26 (1.13–1.42) ^a	1.03 (0.84–1.26)
Other demographic and surgical characteristics			
Age	0.98 (0.95–1.01)	1.01 (0.98–1.03)	1.00 (0.96–1.04)
BMI	1.02 (0.98–1.07)	1.02 (0.98–1.06)	1.00 (0.94–1.07)
Hispanic ethnicity	2.25 (1.17–4.35) ^a	1.92 (1.06–3.46) ^a	0.72 (0.21–2.48)
Race			
White	—	—	—
Black	Not estimable	0.91 (0.63–2.27)	0.42 (0.06–3.14)
Other	0.80 (0.28–2.32)	1.13 (0.50–2.54)	Not estimable
Education			
Less than high school	—	—	—
High school/GED	0.63 (0.28–1.42)	0.40 (0.20–0.80) ^a	0.90 (0.30–2.69)
Some college/associate	0.47 (0.20–1.11)	0.49 (0.25–0.97) ^a	0.39 (0.11–1.39)
4-y college degree	0.47 (0.19–1.14)	0.27 (0.12–0.60) ^a	0.52 (0.15–1.81)
Graduate/professional	0.42 (0.16–1.15)	0.38 (0.17–0.86) ^a	0.81 (0.23–2.81)
Private insurance	0.58 (0.35–0.98) ^a	0.55 (0.35–0.85) ^a	0.55 (0.27–1.11) ^b
Smoker	0.64 (0.35–1.15)	0.84 (0.52–1.35)	1.66 (0.85–3.26)
Vaginal parity	1.19 (1.02–1.40) ^a	1.24 (1.08–1.42) ^a	1.11 (0.89–1.38)
Previous POP surgery	0.98 (0.35–2.78)	1.74 (0.77–3.93)	0.91 (0.25–3.41)

Weston. Prolapse phenotypes and 12-month postoperative prolapse recurrence. Am J Obstet Gynecol 2026.

(continued)

TABLE 5
Associations between baseline patient characteristics and primary and secondary outcomes, adjusted for prolapse severity (POP-Q stage II vs stage III/IV) and previous hysterectomy and with a random intercept for the original study
(continued)

Variable	Symptomatic recurrence	Anatomic recurrence	New or worsening SUI
Previous SUI surgery	0.40 (0.05–3.13)	1.62 (0.55–4.77)	1.10 (0.14–8.88)
Baseline SUI symptoms	0.99 (0.59–1.66)	0.81 (0.52–1.26)	0.12 (0.04–0.36) ^a
Apical surgery performed			
Uterosacral ligament suspension	0.78 (0.44–1.39)	0.91 (0.55–1.49)	1.91 (0.67–5.51)
Sacrospinous ligament fixation	—	—	—
Concurrent MUS	0.81 (0.48–1.37)	0.81 (0.51–1.28)	0.10 (0.05–0.24) ^a

Data are presented as odds ratios (95% confidence intervals) using logistic regression models, adjusted for prolapse severity (POP-Q stage II vs stage III/IV) and previous hysterectomy.

A, isolated anterior; AC, anterior-predominant and apical; AP, anterior and posterior; APC, anterior and posterior and apical; BMI, body mass index; C, isolated apical; GED, General Education Development; GH, genital hiatus; MUS, midurethral sling; P, isolated posterior; PC, posterior-predominant and apical; POP, pelvic organ prolapse; POP-Q, Pelvic Organ Prolapse Quantification; SUI, stress urinary incontinence; SUI, stress urinary incontinence; TVL, total vaginal length.

^a Statistically significant result at $P < .05$; ^b $P < .10$.

Weston. Prolapse phenotypes and 12-month postoperative prolapse recurrence. *Am J Obstet Gynecol* 2026.

in this study population was not predictive of 12-month prolapse recurrence after USLS and SSLF, our results contribute to a growing and important body of research that is focused on better understanding how baseline anatomic parameters (beyond POP-Q stage) in patients with POP may affect surgical results.

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