JAMA | Original Investigation

Effect of Uterosacral Ligament Suspension vs Sacrospinous Ligament Fixation With or Without Perioperative Behavioral Therapy for Pelvic Organ Vaginal Prolapse on Surgical Outcomes and Prolapse Symptoms at 5 Years in the OPTIMAL Randomized Clinical Trial

J. Eric Jelovsek, MD, MMEd; Matthew D. Barber, MD, MHS; Linda Brubaker, MD, MS; Peggy Norton, MD; Marie Gantz, PhD; Holly E. Richter, PhD, MD; Alison Weidner, MD; Shawn Menefee, MD; Joseph Schaffer, MD; Norma Pugh, MS; Susan Meikle, MD, MSPH; for the NICHD Pelvic Floor Disorders Network

IMPORTANCE Uterosacral ligament suspension (ULS) and sacrospinous ligament fixation (SSLF) are commonly performed pelvic organ prolapse procedures despite a lack of long-term efficacy data.

OBJECTIVE To compare outcomes in women randomized to (1) ULS or SSLF and (2) usual care or perioperative behavioral therapy and pelvic floor muscle training (BPMT) for vaginal apical prolapse.

DESIGN, SETTING, AND PARTICIPANTS This 2 × 2 factorial randomized clinical trial was conducted at 9 US medical centers. Eligible participants who completed the Operations and Pelvic Muscle Training in the Management of Apical Support Loss Trial enrolled between January 2008 and March 2011 and were followed up 5 years after their index surgery from April 2011 through June 2016.

INTERVENTIONS Two randomizations: (1) BPMT (n = 186) or usual care (n = 188) and (2) surgical intervention (ULS: n = 188 or SSLF: n = 186).

MAIN OUTCOMES AND MEASURES The primary surgical outcome was time to surgical failure. Surgical failure was defined as (1) apical descent greater than one-third of total vaginal length or anterior or posterior vaginal wall beyond the hymen or retreatment for prolapse (anatomic failure), or (2) bothersome bulge symptoms. The primary behavioral outcomes were time to anatomic failure and Pelvic Organ Prolapse Distress Inventory scores (range, 0-300).

RESULTS The original study randomized 374 patients, of whom 309 were eligible for this extended trial. For this study, 285 enrolled (mean age, 57.2 years), of whom 244 (86%) completed the extended trial. By year 5, the estimated surgical failure rate was 61.5% in the ULS group and 70.3% in the SSLF group (adjusted difference, −8.8% [95% CI, −24.2 to 6.6]). The estimated anatomic failure rate was 45.6% in the BPMT group and 47.2% in the usual care group (adjusted difference, −1.6% [95% CI, −21.2 to 17.9]). Improvements in Pelvic Organ Prolapse Distress Inventory scores were −59.4 in the BPMT group and −61.8 in the usual care group (adjusted mean difference, 2.4 [95% CI, −13.7 to 18.4]).

CONCLUSIONS AND RELEVANCE Among women who had undergone vaginal surgery for apical pelvic organ vaginal prolapse, there was no significant difference between ULS and SSLF in rates of surgical failure and no significant difference between perioperative behavioral muscle training and usual care on rates of anatomic success and symptom scores at 5 years. Compared with outcomes at 2 years, rates of surgical failure increased during the follow-up period, although prolapse symptom scores remained improved.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT01166373

JAMA. 2018;319(15):1554-1565. doi:10.1001/jama.2018.2827

Supplemental content

CME Quiz at jamanetwork.com/learning

Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: The NICHD Pelvic Floor Disorders Network members are listed at the end of this article.

Corresponding Author: J. Eric Jelovsek, MD, MMEd, Duke University, Obstetrics & Gynecology, 209 Baker House, DUMC 3084, Durham, NC 27710 (eric.jelovsek@duke.edu).

Pelvic organ prolapse (POP) is downward descent of the female bladder, uterus, or posthysterectomy vaginal cuff and the small or large bowel, resulting in protrusion of the vagina, uterus, or both.[1] Vaginal surgical repairs of POP are effective and relatively low-risk operations, and the lifetime risk of any primary surgery for POP is 20.0% by the age of 80 years.[2,3] Given the aging population in the United States, the number of women experiencing POP will increase by approximately 50% by 2050.[4] Outcome studies more than 2 years after vaginal surgery are rare and limited by retrospective, noncomparative designs and poor follow-up.[5,6]

Until recently, to our knowledge, there have been no comparative data regarding the 2 most common transvaginal procedures for apical POP, sacrospinous ligament fixation (SSLF) and uterosacral ligament vaginal vault suspension (ULS).[6] The Operations and Pelvic Muscle Training in the Management of Apical Support Loss (OPTIMAL) Trial was a 2 × 2 factorial trial comparing 2-year outcomes in women undergoing vaginal apical prolapse repair with midurethral sling for stress urinary incontinence.[7] There were 2 randomized assignments: (1) perioperative behavioral therapy with pelvic floor muscle training (BPMT) vs usual care and (2) surgical intervention (either ULS or SSLF). Anatomic, functional, and adverse event outcomes were not significantly different between the surgical groups, and no benefit was seen from BPMT on urinary incontinence symptoms at 6 months or prolapse outcomes at 2 years.[8] There were statistically and clinically significant improvements in quality of life, sexual function, and body image at 2 years without group differences.[9]

The Extended-OPTIMAL (E-OPTIMAL) Study followed up participants in the original trial 5 years from surgery to compare surgical failure, changes in quality of life, and complication rates of the 2 surgical and 2 behavioral treatment groups.

Key Points

Question What are the 5-year outcomes associated with uterosacral ligament suspension or sacrospinous ligament fixation with perioperative behavioral therapy and pelvic floor muscle training compared with usual care for women undergoing vaginal prolapse surgery?

Findings The estimated probability of surgical failure was 61.5% with uterosacral ligament suspension vs 70.3% with sacrospinous ligament fixation, a nonsignificant difference. Anatomic failure was 48% with perioperative behavioral therapy and pelvic floor muscle training and 49.5% with usual care, while Prolapse Organ Prolapse Distress Inventory scores improved by −59.4 points vs −61.8 points, respectively, signifying nonsignificant differences.

Meaning Vaginal surgery for prolapse failure rates are high despite maintenance of improved prolapse symptoms.

Methods

Eligible participants for the original trial included women who were planning vaginal surgery for stages 2 through 4 prolapse (vaginal or uterine descent 1 cm proximal to the hymen or beyond) (**Figure 1**), vaginal bulge symptoms, descent of the uterus or vaginal apex at least halfway into the vagina, stress urinary incontinence symptoms, and objective demonstration of stress incontinence by office or urodynamic testing in the previous 12 months.[7,8] Randomization to BPMT or usual care was stratified by site, and randomization to surgical intervention was stratified by surgeon and concomitant hysterectomy. Separate randomization schedules were generated by the data coordination center using random permuted blocks. Participants in the original trial were followed up for 24 months after surgery.

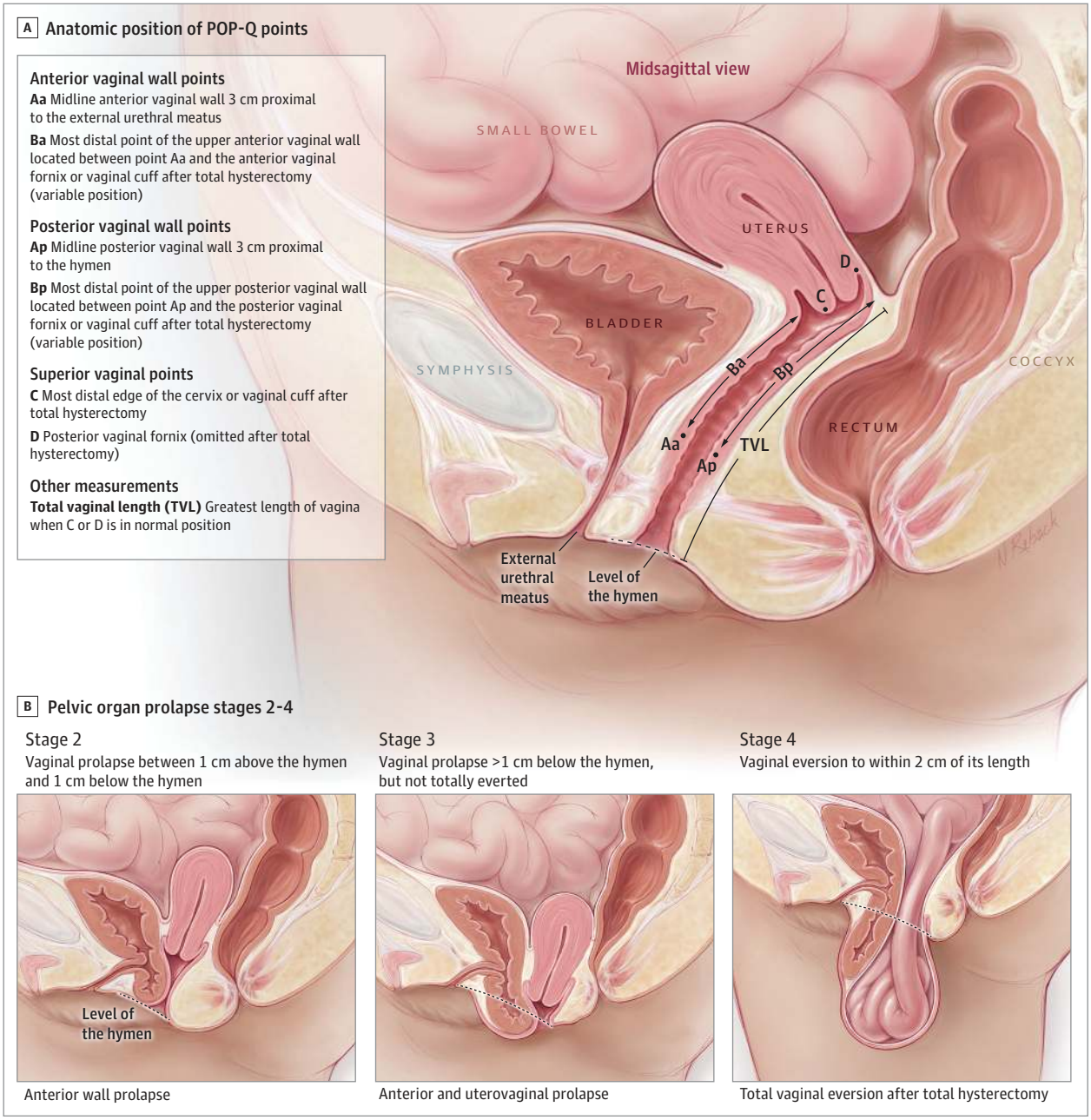
Enrollment in the original trial was from January 2008 to March 2011. Of participants who completed their 24-month original trial visit, women were excluded if unable to provide informed consent or if they were long-term residents of a skilled nursing facility. Participants unable to return for annual visits were not excluded if they participated in the telephone interview portion of the study. After providing written informed consent, eligible participants who completed the original trial enrolled between April 2010 and February 2013 were followed up 5 years after their index surgery from April 2011 through June 2016. Institutional review board approval of this extended trial protocol was granted at each site. Race and ethnicity were collected based on categories on the case report form and choices were selected by participants. The full trial protocol and statistical analysis plan are available in Supplement 1 and Supplement 2.

Study Interventions

As previously described,[7,8] original trial participants underwent standardized surgery for POP consisting of a unilateral SSLF procedure[10,11] or a bilateral ULS procedure.[12] If a participant had uterine prolapse, she underwent a vaginal hysterectomy. Both apical suspension procedures used 2 permanent and 2 delayed absorbable sutures (4 sutures total). All participants underwent a retropubic midurethral sling for stress urinary incontinence. Additional procedures were performed at the surgeon's discretion.

Participants randomized to perioperative BPMT visited centrally trained pelvic floor therapists 2 to 4 weeks before and 2, 4, 6, 8, and 12 weeks after surgery. Each participant practiced pelvic floor muscle exercises and received individualized education on behavioral strategies to reduce urinary and colorectal symptoms during each visit.[7,8] The first visit included evaluation of the patient's pelvic floor muscle function via vaginal palpation, instruction on correct pelvic floor muscle exercise, and recommendations for preoperative pelvic floor muscle exercises. Verbal and written instructions were individualized with a maximum of 45 contractions per day, an initial muscle contraction duration ranging from 1 to 3 seconds, a schedule to increase the contraction duration 1 to 2 seconds per week to a maximum of 7 seconds, and instructions for resuming exercises postoperatively. At the 2-week, 4- to 6-week, and 8-week postoperative visits, the interventionist adjusted the patient's exercise regimen

Figure 1. Pelvic Organ Prolapse Quantification (POP-Q) Stages



The POP-Q points[13] are used to assess a woman's stage of pelvic organ prolapse on examination. The locations of these points are shown in panel A. This panel shows normal anatomy, most frequently seen in nulliparous women. In this trial, eligible patients included women planning vaginal surgery for stages 2 through 4 vaginal prolapse, illustrated in panel B. Descent of POP-Q point C with the Valsalva maneuver more than one-third of the total vaginal length and location of POP-Q points Aa, Ba, Ap, or Bp with the Valsalva maneuver beyond the hymen were among the criteria for surgical failure in this trial.

by gradually increasing the number (maximum ranging from 45 to 60 per day) and duration (maximum = 10 seconds) of each contraction. At the final postoperative session, the interventionist provided patients with a maintenance exercise program consisting of 15 contractions per day at the maximum contraction duration achieved during the intervention period.[7,8]

In-person evaluation at the clinical site and telephone interviews conducted by the central facility at the data coordinating center were performed annually during postoperative years 3 through 5. Each visit and interview occurred within 3 months of the anniversary of the index surgery. Site telephone follow-up for original and extended trial participants occurred approximately 6 months after the initial surgery and yearly thereafter. Evaluators of outcome assessments remained masked to surgical and BPMT randomizations. Participant masking to the surgical intervention continued until all trial participants completed the study.

Outcomes

Surgical Intervention

The primary outcome for this extended trial was the time-to-event outcome of surgical failure up to 5 years after surgery. Measurement of prolapse was based on the Pelvic Organ Prolapse Quantification (POP-Q) system (Figure 1).[13] Surgical failure was present if any of the following criteria were met: (1) POP-Q point C descended with the Valsalva maneuver more than one-third of the total vaginal length; (2) POP-Q points Aa, Ba, Ap, or Bp with the Valsalva maneuver were beyond the hymen; (3) bothersome bulge symptoms were reported by the participant in response to the questions, "Do you usually have a sensation of bulging or protrusion from the vaginal area?" or "Do you usually have a bulge or something falling out that you can see or feel in the vaginal area?" on the Pelvic Floor Disorders Inventory (PFDI)[14]; or (4) the participant received surgery or elected to use a pessary for prolapse at any point during follow-up.

Secondary outcomes of the surgical intervention included anatomic measures of the anterior, posterior, and apical vaginal compartment; time to anatomic failure (defined as POP-Q points Aa, Ba, Ap, or Bp beyond the hymen; point C descending >one-third of total vaginal length, or retreatment); time to bothersome bulge symptoms; and the Pelvic Organ Prolapse Distress Inventory (POPDI; range, 0-300; minimum important clinical difference, 11 points[15]), Urinary Distress Inventory (UDI; range, 0-300; minimum important clinical difference, 11 points[16]), and Colorectal-Anal Distress Inventory (CRADI; range, 0-400; minimum important clinical difference, 11 points[17]) subscales of the PFDI (higher scores indicate worse symptoms)[14]; Patients Global Impression of Improvement (PGI-I)[18]; reoperations and retreatments for pelvic floor disorders; and long-term adverse events specific to the surgical procedures including vaginal granulation tissue and erosion of suture or sling. Pelvic Floor Impact Questionnaire[14] scores, urinary incontinence severity,[19] reoperations and retreatments for stress and urge urinary incontinence, voiding dysfunction, defecatory dysfunction, fecal incontinence, rates of complications[20] including vaginal or perineal stricture, and pelvic muscle strength[21] were also collected but not reported.

Behavioral Intervention

The primary outcomes for the BPMT intervention were time to anatomic failure (defined as POP-Q points Aa, Ba, Ap, or Bp beyond the hymen, point C descending >one-third of total vaginal length, or retreatment) and change from baseline (preoperative) POPDI scores. Secondary outcomes were similar to the surgical intervention.

Sample Size

The estimated sample size for the original trial was 340 randomized participants (170 per surgical treatment group) to provide 80% power for differentiating failure rates of 30% and 17% (success rates of 70% and 83%) using a 2-tailed 5% level of significance using the dichotomous definition of surgical failure 2 years after surgery.[8] A total of 400 participants were expected to be enrolled (200 per group) in the original trial, accounting for a projected 15% dropout or loss to follow-up rate over 2 years. Based on the enrollment and attrition in a long-term study following women treated for prolapse by abdominal sacral colpopexy, we conservatively assumed that at least 75% of participants in the original trial (n = 255) would enroll in this extended trial and the annual dropout or loss to follow-up rate would be approximately 5%.[22] As such, we anticipated approximately 218 participants (109 participants in each of the 2 surgical groups) would provide year 5 data for the extended trial.

Assuming time to surgical failure followed an exponential distribution and fixed follow-up on each participant for 5 years, there was 80% power to detect a hazard ratio of 0.52 based on the anticipated 2-year surgical failure rates of 17% and 30% in the ULS and SSLF groups, respectively, with a 2-sided type I error of 5% with only 167 participants. We assumed that clinically relevant differences in comparisons of continuous variables, including POP-Q measurements[23] and quality-of-life scores, would likely also be detectable with this sample size.[15-17] Assuming 218 participants were followed up for 5 years with equal numbers in each treatment group, we would have 80% power to detect effect sizes of 0.38 in continuous outcomes with a 2-sided type I error of 5%.

Statistical Methods

Participant characteristics at the start of the parent study were compared between treatment groups for women who enrolled in the extended study. Unadjusted confidence intervals for the differences between treatment groups were estimated from *t* tests for continuous variables and from exact tests based on the binomial probability function for categorical variables. Women who enrolled in the extended trial were compared with original trial participants who did not enroll using the same methods.

Kaplan-Meier survival curves were created for descriptive purposes using the midpoint of the censoring interval to estimate the unadjusted probabilities of surgical and anatomic failure, absence of bothersome bulge symptoms, and retreatment of prolapse.

The primary analysis was conducted using an intention-to-treat principle as closely as possible by analyzing all successfully followed up participants in the treatment group to which they were randomized. Although power calculations were based on the extended trial population, all original trial participants were included in the analysis of the time-to-event outcomes of the extended trial to optimize power and minimize bias. Participants with missing data at time points up to 5 years who were not classified as failures were censored at the last time point at which they were classified as successes. Analyses of these variables were performed using accelerated failure time frailty models for interval censored data because outcomes were assessed annually. To accommodate different patterns of failure between the treatment groups, separate survival curves were fit for each group.

The surgical randomization was stratified by concomitant hysterectomy and surgeon, and the BPMT randomization was stratified by center. Therefore, models comparing

the surgical groups included BPMT group and concomitant or prior hysterectomy as independent variables and surgeon as a random frailty effect to account for correlation between outcomes of patients treated by the same surgeon. Models comparing the BPMT groups included an independent variable for surgical group and a frailty effect for center. Once a participant met failure criteria, she remained in that category for all subsequent points. Survival curves for the 2 treatments were compared by estimating the differences between the survival probabilities of the groups at 6 months and 1, 2, 3, 4, and 5 years following surgery. Time to retreatment was not analyzed using accelerated failure time modeling due to the small number of women who underwent retreatment; instead, retreatment by 5 years was analyzed using the methods for categorical outcomes described here. Statistical tests were 2-sided, and significance was evaluated at an α level of .05. No adjustments were made for performing multiple statistical tests; however, comparisons of secondary outcomes were considered exploratory.

All other outcomes were analyzed in the group of women consenting to this extended trial. Analyses of secondary outcomes included all known outcomes and excluded missing data. Differences between treatment groups were evaluated for binary outcomes using binomial regression with an identity link function to estimate risk differences. Because there were small numbers of women with these outcomes, models included only terms for surgical group, BPMT treatment assignment, and their interaction. Changes from baseline in continuous outcomes were compared using general linear models.

Models to compare surgical treatments included the stratification factor of concomitant hysterectomy and a random effect for surgeon, while models to compare BPMT treatment groups included the stratification factor of clinical site as an independent variable. For outcomes for which data were available at multiple points (eg, outcomes at 6 months and yearly intervals following surgery), a longitudinal extension to the model including terms for time as a categorical variable, interactions between BPMT and surgical treatments and time, and a random effect to model the covariance of repeated measures on the same participant was used, and treatment groups were compared at each point. All statistical modeling was conducted with SAS software (version 9.4; SAS Institute Inc).

Results

The original study randomized 374 patients and 309 were eligible for this extended trial. A total of 285 were randomized and 244 (86%) completed the trial. A total of 285 participants (76.2%) from the original trial enrolled in this extended trial; the remaining 89 participants (23.8%) were ineligible or declined enrollment. **Figure 2** shows the flow of participants through the study. **Table 1** displays baseline participant characteristics for women in the extended trial. Among those enrolled in the extended trial, ULS participants had a higher mean number of vaginal deliveries compared with SSLF participants. Most demographics were not significantly different for participants who declined enrollment in the extended study. However, original trial participants were statistically less likely to enroll in the extended trial if they were not black or had met the original trial anatomic failure or POP retreatment criteria (Table 1 and eTable in Supplement 3).

Primary Outcome of Surgical Intervention

Surgical failure rates gradually increased over the follow-up period (**Table 2**; **Figure 3**; eFigure 1 in Supplement 3). The estimated median time to failure was 1.8 years for SSLF and 2.6 years for ULS. By year 5, the estimated proportions of women with surgical failure for the ULS group and the SSLF group, respectively, were 61.5% and 70.3% (difference, −8.8%; [95% CI, −24.2 to 6.6]). The estimated proportions with anatomic failure were 47.5% and 61.8%, respectively (difference, −14.3% [95% CI, −32.1 to 3.5]), and with bothersome bulge symptoms they were 37.4% and 41.8%, respectively (difference, −4.4% [95% CI, −21.3 to 12.5]). The 145 failures based on POP-Q measures involved the apex only (27%), anterior or posterior compartment only (34%), or both apex and anterior/posterior compartments (39%).

Post hoc analysis revealed 50 (34.5%) of the 145 POP-Q failures, 36 (30%) of the 120 participants with bothersome bulge symptoms, and 65 (32.8%) of the 198 total surgical failures subsequently met criteria for the composite definition of success at the participant's last clinic visit without additional treatment but were categorized as failures using the time-to-event analysis. The proportion of women undergoing retreatment for prolapse by 5 years was 11.9% for ULS and 8.1% for SSLF (adjusted risk difference [ARD], 3.9% [95% CI, −3.8 to 11.5]), including pessary (6.0% and 4.5%) and repeat surgery (8.5% and 4.6%); 2.5% and 1.0%, respectively, were treated with both.

Secondary Outcomes of Surgical Intervention

PFDI scores are summarized in eFigure 2 in Supplement 3. Quality of life significantly improved and exceeded minimum clinically important differences from before surgery to 5 years after surgery in both the ULS and SSLF groups including prolapse distress (POPDI, −67.6 and −74.2, respectively; adjusted mean difference [AMD], 6.6 [95% CI, −9.5 to 22.7]), urinary distress (UDI, −75.8 and −80.3, respectively; AMD, 4.5 [95% CI, −10.3 to 19.3]), and for colorectal-anal distress (CRADI, −41.7 and −44.5, respectively; AMD, 2.8 [95% CI, −16.1 to 21.7]). These within-group improvements were maintained over the 5-year follow-up and continued despite the increase in surgical failure rates over time. No statistically significant differences were detected between surgical groups in the PGI-I, with improvement maintained over time indicated by reporting "very much better" or "much better" in 82 (64.1%) and 75 (60.5%) at 3 years, 71 (63.4%) and 65 (59.1%) at 4 years, and 66 (56.9%) and 59 (54.1%) at 5 years for ULS and SSLF, respectively.

Granulation tissue was higher in the ULS group than the SSLF group (ARD, 10.5% [95% CI, −0.2% to 21.2%]) with no significant differences in suture or mesh erosion/exposure between surgical groups (**Table 3**). After the index surgery,

Figure 2. Operations and Pelvic Muscle Training in the Management of Apical Support Loss (OPTIMAL) and Extended OPTIMAL Participant Flow[a]

BPMT indicates behavioral therapy and pelvic floor muscle training; POP-Q, Pelvic Organ Prolapse Quantification System; SSLF, sacrospinous ligament fixation; ULS, uterosacral ligament suspension.

[a] Complete CONSORT diagram can be found in the study by Barber et al.[8]

[b] A total of 77 had anatomic failure at 2 years in OPTIMAL, but only 76 attended the clinic visit; 1 had anatomic failure based on retreatment by 1 year.

[c] Represents a late 2-year visit excluded from original trial analysis but included for the extended trial.

most adverse events occurred in the first 2 years and all 9 participants (3.2%) who underwent subsequent continence surgery did so within 2 years.

Primary Outcome of the Behavioral Intervention

There were no significant differences in outcomes between the BPMT or usual care groups. By year 5, the estimated

Table 1. Baseline Characteristics of the Extended Study Operations and Pelvic Muscle Training in the Management of Apical Support Loss Study Population

Characteristic	No. (%)		ULS vs SSLF Unadjusted Difference, % (95% CI)[a]	No. (%)		BPMT vs Usual Care Unadjusted Difference, % (95% CI)[a]
	ULS (n = 147)	SSLF (n = 138)		BPMT (n = 141)	Usual Care (n = 144)	
Age, mean (SD), y	57.4 (10.9)	56.9 (10.8)	0.5 (−2.0 to 3.0)	57.0 (10.8)	57.4 (10.9)	−0.4 (−2.9 to 2.2)
Race/ethnicity						
White	124 (84.4)	114 (82.6)	1.7 (−9.9 to 13.4)	117 (83.0)	121 (84.0)	−1 (−12.8 to 10.7)
Black	11 (7.5)	10 (7.2)	0.2 (−11.4 to 11.8)	14 (9.9)	7 (4.9)	5.1 (−6.7 to 16.5)
Asian	0 (0.0)	2 (1.4)	−1.4 (−13 to 10.2)	0 (0.0)	2 (1.4)	−1.4 (−13 to 10.2)
American Indian/Alaska Native	0 (0.0)	2 (1.4)	−1.4 (−13 to 10.2)	1 (0.7)	1 (0.7)	0 (−11.6 to 11.6)
Other	12 (8.2)	10 (7.2)	0.9 (−10.7 to 12.5)	9 (6.4)	13 (9.0)	−2.6 (−14.4 to 8.8)
Hispanic ethnic group	31 (21.1)	25 (18.1)	3 (−8.7 to 14.5)	28 (19.9)	28 (19.4)	0.4 (−11.3 to 12.2)
Insurance status						
Private or HMO	99 (67.3)	92 (66.7)	0.7 (−10.9 to 12.3)	97 (68.8)	94 (65.3)	3.5 (−8.1 to 15.1)
Medicaid or Medicare	44 (29.9)	37 (26.8)	3.1 (−8.5 to 14.7)	39 (27.7)	42 (29.2)	−1.5 (−13 to 10.2)
Self-pay	3 (2.0)	3 (2.2)	−0.1 (−11.7 to 11.5)	3 (2.1)	3 (2.1)	0 (−11.6 to 11.6)
Other	28 (19.0)	26 (18.8)	0.2 (−11.4 to 11.8)	25 (17.7)	29 (20.1)	−2.4 (−14.1 to 9.4)
No. of previous deliveries, mean (SD)						
Vaginal	3.3 (2.1)	2.7 (1.6)	0.6 (0.2 to 1.0)	3.1 (2.0)	2.8 (1.7)	0.3 (−0.1 to 0.8)
Cesarean	0.1 (0.5)	0.1 (0.5)	−0.0 (−0.1 to 0.1)	0.1 (0.5)	0.1 (0.4)	0.0 (−0.1 to 0.1)
Menopausal status						
Premenopausal	43 (29.3)	39 (28.3)	1 (−10.6 to 12.6)	42 (29.8)	40 (27.8)	2 (−9.5 to 13.7)
Postmenopausal	98 (66.7)	90 (65.2)	1.4 (−10.2 to 13)	91 (64.5)	97 (67.4)	−2.8 (−14.4 to 8.8)
Not sure	6 (4.1)	9 (6.5)	−2.4 (−14 to 9.2)	8 (5.7)	7 (4.9)	0.8 (−10.9 to 12.3)
Estrogen use						
Oral or patch	17 (11.6)	19 (13.8)	−2.2 (−13.8 to 9.5)	18 (12.8)	18 (12.5)	0.3 (−11.5 to 11.9)
Vaginal	38 (25.9)	29 (21.0)	4.8 (−6.8 to 16.4)	33 (23.4)	34 (23.6)	−0.2 (−11.8 to 11.6)
Current smoker	10 (6.8)	13 (9.4)	−2.6 (−14.2 to 9)	13 (9.2)	10 (6.9)	2.3 (−9.5 to 13.7)
Diabetes	16 (11.0)	14 (10.6)	0.4 (−11.4 to 12.1)	20 (14.6)	10 (7.1)	7.5 (−4.3 to 19.2)
Connective tissue disease	4 (2.8)	1 (0.7)	2 (−9.7 to 13.8)	2 (1.4)	3 (2.1)	−0.7 (−12.7 to 11.3)
Prior procedure						
Hysterectomy	36 (24.5)	38 (27.5)	−3 (−14.6 to 8.6)	31 (22.0)	43 (29.9)	−7.9 (−19.2 to 3.9)
SUI surgery	5 (3.4)	5 (3.6)	−0.2 (−11.8 to 11.4)	3 (2.1)	7 (4.9)	−2.7 (−14.4 to 8.8)
POP surgery	6 (4.1)	12 (8.7)	−4.6 (−16.2 to 7)	6 (4.3)	12 (8.3)	−4.1 (−15.8 to 7.4)
BMI, mean (SD)	28.5 (5.0)	29.2 (6.0)	−0.7 (−2.0 to 0.5)	29.5 (5.8)	28.2 (5.2)	1.3 (0 to 2.5)
Pelvic Organ Prolapse-Q stage[b]						
2	57 (38.8)	50 (36.2)	2.5 (−9.1 to 14.1)	53 (37.6)	54 (37.5)	0.1 (−11.6 to 11.6)
3	86 (58.5)	80 (58.0)	0.5 (−11.1 to 12.2)	84 (59.6)	82 (56.9)	2.6 (−8.9 to 14.4)
4	4 (2.7)	8 (5.8)	−3.1 (−14.7 to 8.6)	4 (2.8)	8 (5.6)	−2.7 (−14.4 to 8.8)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); BPMT, behavioral therapy and pelvic floor muscle training; HMO, health maintenance organization; POP, pelvic organ prolapse; SSLF, sacrospinous ligament fixation, SUI, stress urinary incontinence; ULS, uterosacral ligament suspension.

[a] Confidence intervals for statistical comparisons are from *t* tests for continuous variables and from exact tests based on the binomial probability function for categorical variables.

[b] POP-Q stage 2: the vagina is prolapsed between 1 cm above the hymen and 1 cm below the hymen; stage 3: the vagina is prolapsed more than 1 cm beyond the hymen but less than totally everted; and stage 4: the vagina is everted to within 2 cm of its length.

proportions with anatomic failure for the BPMT group and the usual care group, respectively, were 45.6% and 47.2% (ARD, −1.6% [95% CI, −21.2% to 17.9%]). Estimated median time to failure was 5.7 years for BPMT and 4.8 years for usual care. There were no significant differences in improvement of prolapse distress (POPDI) scores (BPMT, −59.4; usual care, −61.8; AMD, 2.4 [95% CI, −13.7 to 18.4]) between groups despite within-group improvement. There were no significant interactions between the surgical groups (ULS and SSLF) and behavioral interventions (BPMT and usual care).

Secondary Outcomes of the Behavioral Intervention

There were no meaningful differences in the remaining secondary outcomes including the UDI, CRADI, and PGI-I, or adverse events between BPMT or usual care groups.

Table 2. Estimated Adjusted Probability of Pelvic Organ Prolapse Failure After Vaginal Prolapse Surgery

Outcome	No. With Outcome/Total No. (%)[a]		Adjusted Probability of Prolapse (95% CI)[b]		Adjusted Treatment Difference[b]	*P* Value
	ULS	SSLF	ULS	SSLF		
Primary						
Surgical failure[c]						
6 mo	34/177 (19.2)	39/177 (22)	0.237 (0.157 to 0.318)	0.248 (0.154 to 0.343)	−0.011 (−0.135 to 0.113)	.86
1 y	59/177 (33.3)	63/172 (36.6)	0.34 (0.25 to 0.43)	0.376 (0.269 to 0.483)	−0.036 (−0.175 to 0.103)	.60
2 y	76/172 (44.2)	76/166 (45.8)	0.457 (0.358 to 0.555)	0.52 (0.406 to 0.633)	−0.063 (−0.213 to 0.087)	.40
3 y	87/158 (55.1)	89/154 (57.8)	0.527 (0.425 to 0.63)	0.604 (0.489 to 0.718)	−0.076 (−0.23 to 0.078)	.32
4 y	92/150 (61.3)	96/148 (64.9)	0.577 (0.472 to 0.682)	0.661 (0.547 to 0.774)	−0.084 (−0.238 to 0.071)	.28
5 y	94/145 (64.8)	104/146 (71.2)	0.615 (0.508 to 0.722)	0.703 (0.591 to 0.814)	−0.088 (−0.242 to 0.066)	.25
Secondary						
Anatomic failure [d]						
6 mo	24/176 (13.6)	22/176 (12.5)	0.17 (0.094 to 0.246)	0.149 (0.07 to 0.228)	0.021 (−0.088 to 0.131)	.69
1 y	44/175 (25.1)	41/169 (24.3)	0.247 (0.158 to 0.335)	0.262 (0.161 to 0.363)	−0.015 (−0.15 to 0.119)	.82
2 y	54/167 (32.3)	54/163 (33.1)	0.338 (0.236 to 0.441)	0.408 (0.288 to 0.527)	−0.069 (−0.226 to 0.088)	.37
3 y	62/149 (41.6)	66/145 (45.5)	0.397 (0.286 to 0.508)	0.501 (0.374 to 0.628)	−0.104 (−0.272 to 0.065)	.22
4 y	65/139 (46.8)	73/138 (52.9)	0.441 (0.324 to 0.558)	0.568 (0.437 to 0.698)	−0.127 (−0.301 to 0.048)	.15
5 y	68/133 (51.1)	80/134 (59.7)	0.475 (0.354 to 0.597)	0.618 (0.487 to 0.749)	−0.143 (−0.321 to 0.035)	.11
Bothersome bulge symptoms[e]						
6 mo	13/177 (7.3)	22/175 (12.6)	0.08 (0.033 to 0.128)	0.127 (0.053 to 0.201)	−0.046 (−0.135 to 0.042)	.29
1 y	24/172 (14)	40/172 (23.3)	0.141 (0.081 to 0.2)	0.195 (0.103 to 0.286)	−0.054 (−0.164 to 0.056)	.32
2 y	38/165 (23)	51/168 (30.4)	0.226 (0.153 to 0.3)	0.281 (0.172 to 0.39)	−0.055 (−0.188 to 0.078)	.40
3 y	48/146 (32.9)	56/148 (37.8)	0.287 (0.203 to 0.372)	0.339 (0.22 to 0.459)	−0.052 (−0.2 to 0.096)	.48
4 y	53/138 (38.4)	59/144 (41)	0.335 (0.242 to 0.429)	0.383 (0.256 to 0.51)	−0.048 (−0.208 to 0.112)	.54
5 y	56/133 (42.1)	64/134 (47.8)	0.374 (0.273 to 0.476)	0.418 (0.286 to 0.55)	−0.044 (−0.213 to 0.125)	.60

Abbreviations: SSLF, sacrospinous ligament fixation; ULS uterosacral ligament suspension.

[a] Numerator is the number of participants classified at the time point or a prior point as a failure; denominator includes all participants in the numerator plus participants evaluated at the point or a later point as a success who had not previously been classified as a failure.

[b] Based on accelerated failure time, frailty models controlling for behavioral therapy and pelvic floor muscle training group and concomitant or prior hysterectomy as independent variables and surgeon as a random frailty effect.

[c] Surgical failure was defined as Pelvic Organ Prolapse Quantification (POP-Q) point C descended more than one-third of total vaginal length; POPQ points Aa, Ba, Ap, or Bp were beyond the hymen; bothersome vaginal bulge symptoms were reported by the participant; or the participant received retreatment. The apex is point C (cervix), and posteriorly is point D (pouch of Douglas). In women after hysterectomy, point C is the vaginal cuff and point D is omitted.

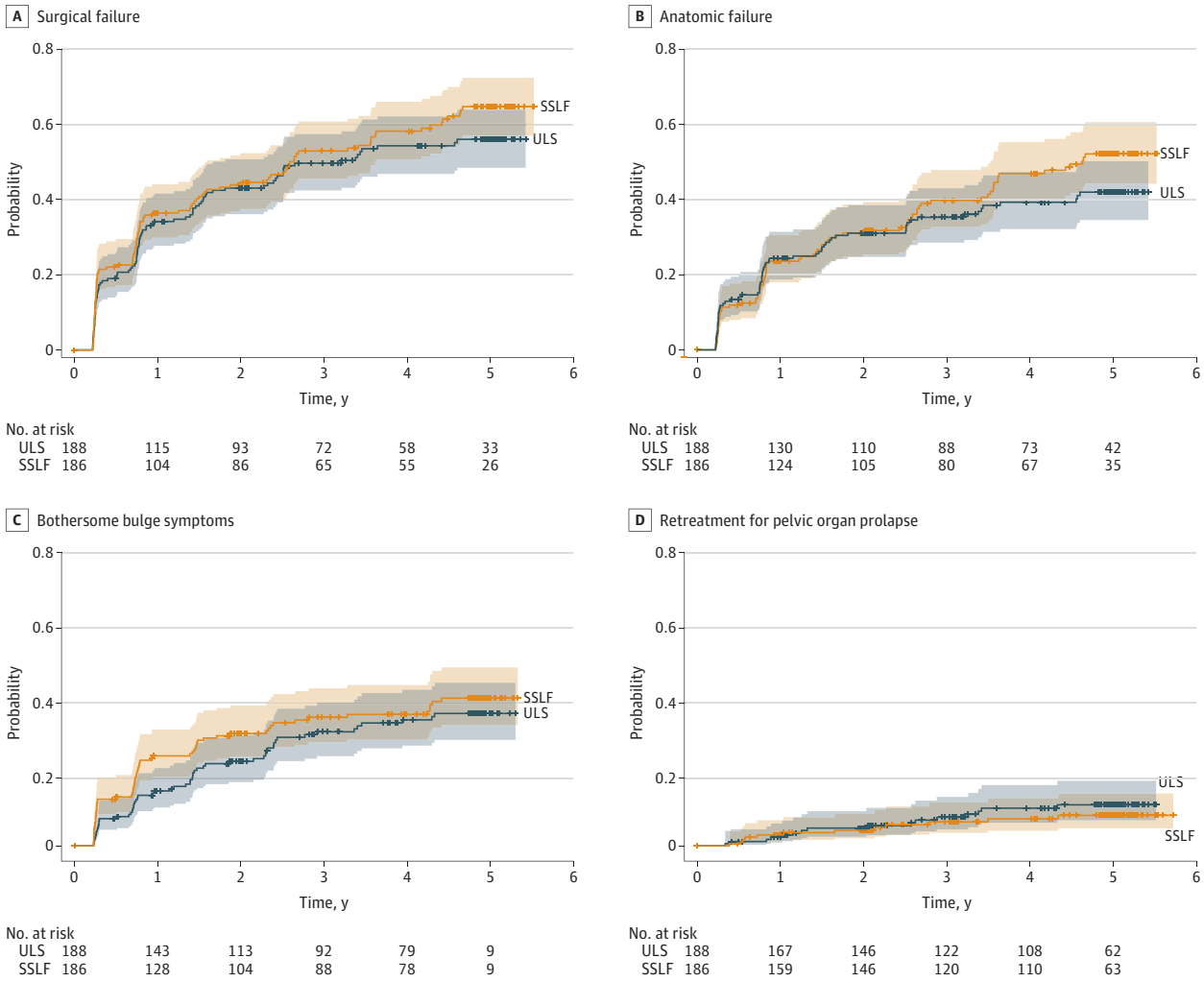
[d] Anatomic failure was defined as POPQ system point C descended more than one-third of total vaginal length; POPQ points Aa, Ba, Ap, or Bp were beyond the hymen; or the participant received retreatment during follow-up.

[e] Bothersome bulge symptoms were reported by the participant in response to the questions, "Do you usually have a sensation of bulging or protrusion from the vaginal area?" or "Do you usually have a bulge or something falling out that you can see or feel in the vaginal area?" on the Pelvic Floor Disorders Inventory.

Discussion

For women undergoing transvaginal native tissue procedures for vaginal apical prolapse (ULS and SSLF), this study provides evidence that these procedures improve prolapse symptoms and quality of life. However, the primary surgical outcome demonstrated there was significant deterioration in success over time, with approximately two-thirds of original trial participants meeting a priori trial definitions of failure 5 years after surgery with no significant difference between ULS and SSLF and no significant difference between perioperative behavioral muscle training and usual care on rates of anatomic failure and symptom scores. Other pelvic organ prolapse surgical trials have demonstrated deterioration in success rates over time but sustained improvement in patient

Figure 3. Kaplan-Meier Survival Curves for Failure of Vaginal Prolapse Surgery by Uterosacral Ligament Suspension or Sacrospinous Ligament Fixation in Treating Pelvic Organ Prolapse Through Year 5



A, The probability of surgical failure was defined as (1) Pelvic Organ Prolapse Quantification System (POP-Q) point C descended more than one-third of total vaginal length; (2) POP-Q points Aa, Ba, Ap, or Bp beyond the hymen; (3) bothersome bulge symptoms reported by the participant; or (4) the participant received retreatment. B, Probability of anatomic failure defined as POP-Q point C descended more than one-third of total vaginal length; POP-Q points Aa, Ba, Ap, or Bp beyond the hymen; or the participant received retreatment during follow-up. POP-Q points Aa and Ap are 3 cm proximal to or above the hymenal ring anteriorly and posteriorly, respectively. Points Ba and Bp are defined as the lowest points of the prolapse between Aa anteriorly or Ap posteriorly and the vaginal apex. The apex is point C (cervix), and posteriorly is point D (pouch of Douglas). In women after hysterectomy, point C is the vaginal cuff and point D is omitted. C, Bothersome bulge symptoms were reported by the participant in response to the questions, "Do you usually have a sensation of bulging or protrusion from the vaginal area?" or "Do you usually have a bulge or something falling out that you can see or feel in the vaginal area?" on the Pelvic Floor Disorders Inventory. D, Probability of Retreatment for Pelvic Organ Prolapse. The + symbol represents a censored participant. SSLF indicates sacrospinous ligament fixation; ULS, uterosacral ligament suspension.

symptoms. For example, 5 to 7 years after abdominal sacrocolpopexy using synthetic mesh, failure was seen in 34% to 48% using a similar outcome definition while POPDI symptom scores remained improved compared with before surgery.[22] This suggests that surgical counseling should convey higher 5-year failure rates in the face of sustained prolapse symptom improvement and avoid implications that a single procedure is curative. Awareness that POP may be a chronic condition can assist patient understanding of the multifactorial contributions to pelvic floor disorder development, set expectations after surgery, and enhance shared decision making during surgical counseling. This trial also highlights the need for long-term follow-up in surgical trials for prolapse as most studies rarely follow up participants beyond 1 year.[6]

As was seen after 2-year follow-up, anatomic and symptom status of participants was not significantly different between SSLF and ULS at 5 years.[8] Both procedures have technical advantages and disadvantages; surgical proficiency in both procedures allows surgeons to provide options based on the anatomic and technical demands of individual patients. It is possible that SSLF could have as much as 24.2%

Table 3. Secondary Outcomes of Cumulative Rates of Granulation Tissue, Suture Exposure, Mesh Erosion or Exposure, and Repeat Surgery

Outcome	No./Total No. (%)		Adjusted Risk Difference, % (95% CI) for ULS vs SSLF at 5 y[a]
	ULS	SSLF	
Granulation tissue			
2 y	32/147 (21.8)	20/138 (14.5)	
3 y	32/136 (23.5)	20/128 (15.6)	
4 y	34/127 (26.8)	20/118 (16.9)	
5 y	35/121 (28.9)	21/112 (18.8)	10.5 (−0.2 to 21.2)
Suture exposure			
2 y	27/147 (18.4)	26/138 (18.8)	
3 y	28/137 (20.4)	27/130 (20.8)	
4 y	30/127 (23.6)	29/122 (23.8)	
5 y	31/120 (25.8)	29/113 (25.7)	0.3 (−10.8 to 11.4)
Midurethral sling erosion or exposure			
2 y	1/147 (0.7)	1/137 (0.7)	
3 y	1/134 (0.7)	3/127 (2.4)	
4 y	1/122 (0.8)	4/117 (3.4)	
5 y	2/113 (1.8)	4/108 (3.7)	−1.9 (−6.2 to 2.4)
Pelvic organ prolapse surgery			
2 y	4/147 (2.7)	2/138 (1.4)	
3 y	7/133 (5.3)	3/126 (2.4)	
4 y	9/117 (7.7)	4/110 (3.6)	
5 y	10/118 (8.5)	5/110 (4.5)	3.9 (−2.5 to 10.3)

Abbreviations: SSLF, sacrospinous ligament fixation; ULS, uterosacral ligament suspension.

[a] Adjusted risk differences are from binomial regression models with an identity link function. Models are adjusted for surgical and behavioral therapy and pelvic floor muscle training treatment assignments and the interaction between them. Due to small numbers, the model for midurethral sling erosion or exposure includes surgical treatment assignment only.

worse surgical failure rate or as much as 6.6% better surgical failure rate than ULS. Optimization of anatomic support following transvaginal surgery remains a top priority for pelvic surgeons. Transvaginal native tissue prolapse surgery has been shown to have lower efficacy than abdominal repairs with mesh (sacrocolpopexy) but is associated with decreased morbidity, making it the procedure of choice for many women.[24,25] The use of synthetic mesh to reinforce transvaginal apical prolapse repairs has been shown to improve some anatomic outcomes but is associated with greater morbidity.[6,26] Thus, the combination of procedures for prolapse in the setting of transvaginal apical repair requires further study to assess whether specific combinations may improve longer-term outcomes. Additionally, there is a need for innovative new treatments to improve long-term outcomes while minimizing risk. While it seemed a promising potential adjunct to surgery, the short-course, perioperative behavioral and pelvic muscle training tested in this trial did not significantly alter patient status at 2 or 5 years.[8]

The threshold for "failure" remains one of the most debated topics in reconstructive pelvic surgery. Although anatomic and symptomatic failure rates as defined in this trial were high, on average, participants demonstrated clinically meaningful improvements in quality of life that were sustained through 5 years. Results also showed that loss of vaginal anatomic support and presence of prolapse symptoms after surgery are not unidirectional and can be dynamic. More than one-third of patients who met criteria for surgical failure by either anatomic or symptom criteria subsequently met criteria for the composite definition of success with successful anatomic support and no prolapse symptoms at later follow-up without reintervention. This suggests the typical time-to-event assumption of "once a failure always a failure" may not hold with POP surgery. This may have the unintended effect of artificially increasing failure rates. Moreover, this has implications for design and analysis of future studies. Despite the limitations of how failure was defined and analyzed, this would have affected both groups.

Five years after a successful operation, patients and surgeons would like to see a continued beneficial effect. However, in this study, despite a high cumulative surgical and anatomic failure rate, participants maintained clinically meaningful improvements in symptoms and quality of life at 5 years and few underwent retreatment during follow-up. This highlights the need to further investigate how failure after prolapse surgery is best defined, particularly from the patient perspective. A greater understanding of patient-centric measures of surgical outcomes, balanced with anatomic surgical goals, is needed for prolapse surgical trials.

In the original trial, the rate of perioperative adverse events was not significantly different between surgical groups, although there was greater risk of transient ureteral kinking after ULS and greater neurologic pain after SSLF.[8] Most adverse events occurred within the first 2 years. With long-term follow-up, ULS was found to have greater risk of vaginal granulation tissue than SSLF.

The findings of this study are strengthened by the randomized, multicentric design of the primary study,[8] the high proportion of participants remaining in follow-up of the extended study, and rigorous longitudinal assessments.

Limitations

This study has several limitations. First, selective dropout and loss to follow-up has the potential to affect the estimates of surgical failure. There was significant participant dropout in the original study and this extended study, and participants with better outcomes were more likely to enroll in the extended study than those with worse outcomes. This could lead to biased estimates of average long-term outcomes, but it is probable that the bias affected both treatment groups similarly, so estimates of comparative effectiveness may be less subject to error. To minimize this bias, original trial participants were included in the analysis of the time-to-event outcomes of the extended trial. Second, the a priori definitions of failure used in this trial may be considered too rigorous in light of available evidence subsequent to the initial original trial design, nearly a decade ago.[27] The selection of surgical outcome measures for prolapse surgery remains a research priority. As data from this trial become publicly available, investigators are encouraged to assess the utility of other failure definitions.

Conclusions

Among women who had undergone vaginal surgery for apical pelvic organ vaginal prolapse, there was no significant difference between ULS and SSLF in rates of surgical failure and no significant difference between perioperative behavioral muscle training and usual care on rates of anatomic success and symptom scores at 5 years. Compared with outcomes at 2 years, rates of surgical failure increased during the follow-up period, although prolapse symptom scores remained improved.

ARTICLE INFORMATION

Accepted for Publication: February 26, 2018.

Author Affiliations: Obstetrics/Gynecology and Women's Health Institute, Cleveland Clinic, Cleveland, Ohio (Jelovsek, Barber); Departments of Obstetrics and Gynecology and Urology, Loyola University Chicago Stritch School of Medicine, Chicago, Illinois (Brubaker); Associate Editor, *JAMA* (Brubaker); Department of Obstetrics and Gynecology, University of Utah, Medical Center, Salt Lake City (Norton); RTI International, Research Triangle Park, North Carolina (Gantz, Pugh); Department of Obstetrics and Gynecology, University of Alabama at Birmingham (Richter); Department of Obstetrics and Gynecology, Duke University, Medical Center, Durham, North Carolina (Weidner); Department of Obstetrics and Gynecology, Southern California Kaiser Permanente, San Diego (Menefee); Department of Obstetrics and Gynecology, University of Texas Southwestern Medical Center, Dallas (Schaffer); Northwest Physician Group, Amarillo, Texas (Meikle).

Author Contributions: Dr Gantz had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Jelovsek, Barber, Brubaker, Norton, Gantz, Richter, Menefee, Schaffer.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Jelovsek, Barber, Brubaker, Gantz, Richter, Weidner, Menefee, Schaffer, Meikle.
Critical revision of the manuscript for important intellectual content: Jelovsek, Barber, Brubaker, Norton, Gantz, Richter, Weidner, Menefee, Schaffer, Pugh.
Statistical analysis: Jelovsek, Gantz, Richter, Pugh.
Obtained funding: Barber, Brubaker, Norton, Richter, Weidner, Schaffer.
Administrative, technical, or material support: Jelovsek, Brubaker, Gantz, Richter, Menefee, Meikle.
Supervision: Jelovsek, Barber, Brubaker, Norton, Gantz, Richter, Menefee, Meikle.

Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Jelovsek reported receiving grants from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Pelvic Floor Disorders Network and royalties from UpToDate. Dr Barber reported receiving royalties from UptoDate and Elsevier. Dr Brubaker reported receiving grants and other funding from the National Institutes of Health (NIH), *JAMA*, *Journal of Female Pelvic Medicine and Reconstructive Surgery*, UpToDate, and the American Board of Obstetrics and Gynecology. Dr Gantz reported receiving grants from the NICHD. Dr Richter reported receiving grants from the NICHD, NIH/Washington University, PCORI/Brown University, UT Southwestern, and Renovia and royalties from UpToDate. Dr Richter was previously on an advisory board for Kimberly-Clark. Dr Weidner reported receiving a grant from the NIH. Dr Menefee reported receiving grants from the NICHD and personal fees from UpToDate. Dr Schaffer reported receiving grants from the NIH and personal fees from Astellas, Boston Scientific, and McGraw-Hill Publishing.

Funding/Support: This study was supported by grants U01 HD041249, U10 HD041250, U10 HD041261, U10 HD041267, U10 HD054136, U10 HD054214, U10 HD054215, U01 HD069031, and U10 HD054241 from the NICHD and the NIH Office of Research on Women's Health.

Role of the Funder/Sponsor: The NICHD project scientist for the Pelvic Floor Disorders Network during this study, Dr Meikle, became the project scientist when the Optimal study was initiated and had a role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Group Information: In addition to the authors, the following members of the Pelvic Floor Disorders Network participated in the Extended Operations and Pelvic Muscle Training in the Management of Apical Support Loss (E-OPTIMAL) Trial: *RTI International, Research Triangle Park, North Carolina (PFDN data coordinating center, July 1, 2011, to present):* Dennis Wallace, Kevin A. Wilson, Daryl Matthews, Tamara L. Terry, Jutta Thornberry, Amanda Youmans-Weisbuch, Ryan E. Whitworth, Michael P. Hieronymus, Lauren Klein Warren, and Benjamin Carper. *University of Michigan, Ann Arbor (PFDN data coordinating center, until July 1, 2011):* Morton Brown, Nancy Janz, John Wei, Xiao Xu, Beverley Marchant, Donna DiFranco, Yang Casher, Kristina Slusser, and Zhen Chen. *Cleveland Clinic, Cleveland, Ohio:* Mark D. Walters, Marie F. R. Paraiso, Beri M. Ridgeway, Ly Pung, Cheryl Williams, Linda McElrath, Betsy O'Dougherty, and Megan Edgehouse. *Loyola University Chicago, Illinois:* Mary Tulke, Elizabeth Mueller, Kimberly Kenton, and Kathleen Jesse. *University of California, San Diego, Health Systems:* Charles W. Nager, Emily Lukacz, Michael E. Albo, Cara Grimes, Heidi W. Brown, Anna C. Kirby, Leah Merrin, JoAnn Columbo, and Nehal Mehta. *Southern California Kaiser Permanente, Downey:* Mercedes Cardona and Eudocia Zapata. *Southern California Kaiser Permanente, San Diego:* John Nguyen, Sharon Jakus-Waldman, Emily L. Whitcomb, Keisha Y. Dyer, Karl M. Luber, Jasmine Tan-Kim, Gouri B. Diwadkar, Lynn M. Hall, Linda M. Mackinnon, and Gisselle Zazueta-Damian. *University of Utah, Salt Lake City:* Ingrid Nygaard, Yvonne Hsu, Jan Baker, Linda Freedman, Linda Griffin, Maria Masters, Amy Orr, and Kristina Heintz. *University of Alabama at Birmingham: Department of Veteran Affairs, Birmingham, Alabama:* Kathryn Burgio, Patricia Goode, and Alayne Markland. *University of Alabama at Birmingham:* R. Edward Varner, Robert Holley, William J. Greer, L. Keith Lloyd, Tracy S. Wilson, Jonathan L. Gleason, Alicia Ballard, Candace Parker-Autry, Lisa Pair, Velria Willis, Nancy Saxon, Lachele Ward, Kathy Carter, and Julie Burge. *Duquesne University, Pittsburg, Pennsylvania:* Diane Borello-France. *Duke University Medical Center, Durham, North Carolina:* Anthony G. Visco, Cindy L. Amundsen, Nazema Y. Siddiqui, Jennifer M. Wu, Mary Raynor, Mary McGuire, and Ingrid Harm-Ernandes. *University of Texas Southwestern Medical Center, Dallas:* David Rahn, Marlene Corton, Clifford Wai, Kelly Moore, Shanna Atnip, Pam Martinez, and Deborah Lawson. *Formerly Eunice Kennedy Shriver National Institute of Child Health and Human Development:* Anne Weber. *PFDN Steering Committee Chair:* Katherine Hartmann. *PFDN Data Safety and Monitoring Board members:* Paul Tulikangas, University of Connecticut Hartford Hospital; Lan Kong, Penn State University College of Medicine; Missy Lavender, Women's Health Foundation; Donna McClish, Virginia Commonwealth University; Katharine O'Dell, UMass Memorial Medical Center; Leslie Rickey, Yale New Haven Hospital; David Shade, Johns Hopkins University; and Ashok Tuteja, University of Utah.

Disclaimer: Dr Brubaker is an Associate Editor of *JAMA* but was not involved in the editorial review or the decision to accept the manuscript for publication.

REFERENCES

1. Jelovsek JE, Maher C, Barber MD. Pelvic organ prolapse. *Lancet*. 2007;369(9566):1027-1038.
2. Wu JM, Matthews CA, Conover MM, Pate V, Jonsson Funk M. Lifetime risk of stress urinary incontinence or pelvic organ prolapse surgery. *Obstet Gynecol*. 2014;123(6):1201-1206.
3. Committee on Practice Bulletins-Gynecology, American Urogynecologic Society. Practice bulletin No. 185: pelvic organ prolapse. *Obstet Gynecol*. 2017;130(5):e234-e250.
4. Wu JM, Vaughan CP, Goode PS, et al. Prevalence and trends of symptomatic pelvic floor disorders in US women. *Obstet Gynecol*. 2014;123(1):141-148.
5. Diwadkar GB, Barber MD, Feiner B, Maher C, Jelovsek JE. Complication and reoperation rates after apical vaginal prolapse surgical repair: a systematic review. *Obstet Gynecol*. 2009; 113(2 pt 1):367-373.
6. Maher C, Feiner B, Baessler K, Christmann-Schmid C, Haya N, Brown J. Surgery for women with apical vaginal prolapse. *Cochrane Database Syst Rev*. 2016;10:CD012376.
7. Barber MD, Brubaker L, Menefee S, et al; Pelvic Floor Disorders Network. Operations and Pelvic Muscle Training in the Management of Apical Support Loss (OPTIMAL) Trial: design and methods. *Contemp Clin Trials*. 2009;30(2):178-189.
8. Barber MD, Brubaker L, Burgio KL, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Pelvic Floor Disorders Network. Comparison of 2 transvaginal surgical approaches and perioperative behavioral therapy for apical vaginal prolapse: the OPTIMAL randomized trial. *JAMA*. 2014;311(10):1023-1034.
9. Lukacz ES, Warren LK, Richter HE, et al. Quality of life and sexual function 2 years after vaginal surgery for prolapse. *Obstet Gynecol*. 2016;127(6): 1071-1079.
10. DeLancey JO, Morley GW, Howard D. Sacrospinous suspension: Michigan 4-wall offers better support. *OBG Management*. 2001;13 (3):18-29.
11. Morley GW, DeLancey JO. Sacrospinous ligament fixation for eversion of the vagina. *Am J Obstet Gynecol*. 1988;158(4):872-881.
12. Shull BL, Bachofen C, Coates KW, Kuehl TJ. A transvaginal approach to repair of apical and other associated sites of pelvic organ prolapse with uterosacral ligaments. *Am J Obstet Gynecol*. 2000; 183(6):1365-1373.
13. Bump RC, Mattiasson A, Bø K, et al. The standardization of terminology of female pelvic organ prolapse and pelvic floor dysfunction. *Am J Obstet Gynecol*. 1996;175(1):10-17.
14. Barber MD, Kuchibhatla MN, Pieper CF, Bump RC. Psychometric evaluation of 2 comprehensive condition-specific quality of life instruments for women with pelvic floor disorders. *Am J Obstet Gynecol*. 2001;185(6):1388-1395.
15. Barber MD, Walters MD, Cundiff GW, Group PT; PESSRI Trial Group. Responsiveness of the Pelvic Floor Distress Inventory (PFDI) and Pelvic Floor Impact Questionnaire (PFIQ) in women undergoing vaginal surgery and pessary treatment for pelvic organ prolapse. *Am J Obstet Gynecol*. 2006;194(5): 1492-1498.
16. Barber MD, Spino C, Janz NK, et al; Pelvic Floor Disorders Network. The minimum important differences for the urinary scales of the Pelvic Floor Distress Inventory and Pelvic Floor Impact Questionnaire. *Am J Obstet Gynecol*. 2009;200(5): 580.e1-7.
17. Jelovsek JE, Chen Z, Markland AD, et al. Minimum important differences for scales assessing symptom severity and quality of life in patients with fecal incontinence. *Female Pelvic Med Reconstr Surg*. 2014;20(6):342-348.
18. Yalcin I, Bump RC. Validation of two global impression questionnaires for incontinence. *Am J Obstet Gynecol*. 2003;189(1):98-101.
19. Sandvik H, Hunskaar S, Seim A, Hermstad R, Vanvik A, Bratt H. Validation of a severity index in female urinary incontinence and its implementation in an epidemiological survey. *J Epidemiol Community Health*. 1993;47(6):497-499.
20. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. 2004; 240(2):205-213.
21. FitzGerald MP, Burgio KL, Borello-France DF, et al; Urinary Incontinence Treatment Network. Pelvic-floor strength in women with incontinence as assessed by the brink scale. *Phys Ther*. 2007;87 (10):1316-1324.
22. Nygaard I, Brubaker L, Zyczynski HM, et al. Long-term outcomes following abdominal sacrocolpopexy for pelvic organ prolapse. *JAMA*. 2013;309(19):2016-2024.
23. Haylen BT, de Ridder D, Freeman RM, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. *Int Urogynecol J*. 2010;21(1):5-26.
24. Maher C, Feiner B, Baessler K, Schmid C. Surgical management of pelvic organ prolapse in women. *Cochrane Database Syst Rev*. 2013;4(4): CD004014.
25. Siddiqui NY, Grimes CL, Casiano ER, et al; Society of Gynecologic Surgeons Systematic Review Group. Mesh sacrocolpopexy compared with native tissue vaginal repair: a systematic review and meta-analysis. *Obstet Gynecol*. 2015;125(1):44-55.
26. Schimpf MO, Abed H, Sanses T, et al; Society of Gynecologic Surgeons Systematic Review Group. Graft and mesh use in transvaginal prolapse repair: a systematic review. *Obstet Gynecol*. 2016;128(1): 81-91.
27. Barber MD, Brubaker L, Nygaard I, et al; Pelvic Floor Disorders Network. Defining success after surgery for pelvic organ prolapse. *Obstet Gynecol*. 2009;114(3):600-609.