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Factorial comparison of two transvaginal surgical approaches and of perioperative behavioral therapy for women with apical vaginal prolapse: The OPTIMAL Randomized Trial

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Abstract

IMPORTANCE—Over 300,000 surgeries are performed annually in the United States for pelvic organ prolapse. Sacrospinous ligament fixation (SSLF) and uterosacral ligament suspension (ULS) are commonly performed transvaginal surgeries to correct apical prolapse. Little is known about their comparative efficacy and safety, and it is unknown whether perioperative behavioral therapy with pelvic floor muscle training (BPMT) improves outcomes of prolapse surgery.

OBJECTIVE—To compare outcomes between 1) SSLF and ULS and 2) perioperative BPMT and usual perioperative care in women undergoing surgery for vaginal prolapse and stress urinary incontinence.

DESIGN, SETTING AND PARTICIPANTS—Multi-center, 2×2 factorial randomized trial of 374 women undergoing surgery to treat both apical vaginal prolapse and stress urinary incontinence was conducted between 2008 and 2013 at 9 U.S. medical centers. Two-year follow-up rate was 84.5%.

INTERVENTIONS—Surgical intervention: Transvaginal surgery including mid-urethral sling with randomization to SSLF (n = 186) or ULS (n=188); Behavioral intervention: Randomization to perioperative BPMT (n = 186) or usual care (n=188).

MAIN OUTCOME MEASURES—The primary outcome for the surgical intervention (surgical success) was defined as: 1) no apical descent greater than one-third into vaginal canal *or* anterior or posterior vaginal wall beyond the hymen (anatomic success); 2) no bothersome vaginal bulge symptoms and 3) no retreatment for prolapse at 2 years. For the behavioral intervention, primary outcome at 6 months was urinary symptom scores (Urinary Distress Inventory; range 0–300, higher scores worse), and primary outcomes at 2 years were prolapse symptom scores (Pelvic Organ Prolapse Distress Inventory; range 0–300, higher scores worse) and anatomic success.

RESULTS—At 2 years, surgical group was not significantly associated with surgical success rates [ULS 59.2% (93/154) vs. SSLF 60.5% (92/152), OR 0.9 (95% CI 0.6, 1.5)] or serious adverse event rates [ULS 16.5% (31/188) vs. SSLF 16.7% (31/186), OR 0.9 (95% CI 0.5, 1.6)]. BPMT was not associated with greater improvements in urinary scores at 6 months [treatment difference −6.7 (95% CI −19.7, 6.2)], prolapse scores at 24 months [treatment difference −8.0 (95% CI −22.1, 6.1)] or anatomic success at 24 months.

CONCLUSIONS AND RELEVANCE—Two years after vaginal surgery for prolapse and stress urinary incontinence, neither ULS nor SSLF was significantly superior to the other for anatomic, functional, and or adverse event outcomes. Perioperative BPMT did not improve urinary symptoms at 6 months or prolapse outcomes at 2 years.

INTRODUCTION

Female pelvic floor disorders are a spectrum of conditions including pelvic organ prolapse and urinary incontinence. Pelvic organ prolapse occurs when the uterus descends into the lower vagina or vaginal walls protrude beyond the vaginal opening. Approximately 300,000 surgeries for prolapse are performed annually in the U.S.[1] Most surgery for pelvic organ prolapse (80–90%) is performed transvaginally, with the remainder performed abdominally.[1–4] Increasingly, surgeons recognize that adequate apical (upper vaginal) support is an essential component of a durable repair.[5–7] The sacrospinous ligament fixation (SSLF) and the uterosacral vaginal vault suspension (ULS) are the two most widely used

vaginal procedures for correcting apical prolapse, yet no comparative data exist about their relative efficacy and safety.[8]

Concurrent pelvic floor disorders are common in women seeking vaginal prolapse surgery. Up to 73% report urinary incontinence, including the common subtype of stress incontinence or involuntary urine loss with coughing, sneezing or physical activity.[9] Following prolapse surgery, new pelvic floor symptoms may develop while pre-existing pelvic floor symptoms may improve, worsen or remain unchanged. As a stand-alone therapy, behavioral therapy with pelvic floor muscle training (BPMT) is an effective treatment for pelvic floor symptoms with incontinence cure rates as high as 78% and improved prolapse stage in up to 17%.[10–14] Diminished pelvic floor muscle strength has been associated with increased risk of prolapse recurrence and reoperation.[15] BPMT, therefore, may be a logical adjunct if it improves surgical outcomes. Two reviews of perioperative physiotherapy for women undergoing prolapse surgery prioritized a need for robust, well-designed trials to evaluate the efficacy of perioperative BPMT.[14,16]

The Operations and Pelvic Muscle Training in the Management of Apical Support Loss (OPTIMAL) trial used a 2×2 factorial design to evaluate 2 primary aims: 1) to compare surgical outcomes of SSLF to ULS 24 months after vaginal surgery for apical or uterine prolapse and stress incontinence and 2) to evaluate the impact of perioperative BPMT on urinary symptoms 6 months after surgery and on anatomic outcomes and prolapse symptoms 24 months after surgery.

METHODS

Study Design

The design of the OPTIMAL trial has been published in detail.[17] This factorial randomized trial was conducted between January 2008 and May 2013 at 9 sites participating in the NIH-sponsored Pelvic Floor Disorders Network. Eligible participants included women ≥18 years undergoing vaginal surgery for Stage 2–4 prolapse (vaginal or uterine descent 1 cm proximal to the hymen or beyond)[18] with a) complaints of vaginal bulge symptoms; b) descent of the uterus or vaginal apex at least half-way into the vagina; c) stress urinary incontinence symptoms; and d) objective demonstration of stress incontinence by office or urodynamic testing in the previous 12 months (See eTable 1 for detailed eligibility criteria). The institutional review boards at each site approved the protocol. All participants provided written informed consent for study participation. Race/ethnicity was obtained by self-report.

Using a 2×2 factorial design, each enrolled patient underwent two distinct randomizations: first, perioperative BPMT or usual care and second, SSLF or ULS. Participants were assigned with equal probability, using a random permuted block design generated by the Data Coordinating Center with the randomized treatment allocations provided in two sequentially numbered, sealed, opaque envelopes (one for randomization to BPMT or usual care, and one for randomization to ULS or SSLF). Randomization to BPMT versus usual care took place preoperatively and was stratified by clinical site. The second randomization to SSLF or ULS took place in the operating room and was stratified by surgeon and concomitant hysterectomy.

Study Interventions

Participants underwent transvaginal surgery for pelvic organ prolapse, including the assigned apical suspension procedure. The SSLF procedure, performed unilaterally, was a modification of the Michigan 4-wall technique.[19,20] The ULS procedure, performed bilaterally, was a modification of the technique described by Shull.[21] Both apical suspension procedures used two permanent and two delayed absorbable sutures (four sutures total).[17] All patients with uterine prolapse underwent vaginal hysterectomy. A concomitant retropubic mid-urethral sling (Tension-Free Vaginal Tape [TVT®]; Ethicon Women's Health and Urology, Somerville, NJ) was performed for stress urinary incontinence. Other concomitant surgeries were performed at the surgeon's discretion; biologic or synthetic graft materials were not allowed for the prolapse repairs.

Usual perioperative care included routine perioperative teaching and standardized postoperative instructions. Participants randomized to perioperative BPMT received an individualized program that included one visit 2–4 weeks prior to surgery, and four post-operative visits (2, 4–6, 8, and 12 weeks after surgery).[17] (eTable 2) Pelvic floor muscle training, individualized progressive pelvic floor muscle exercise, and education on behavioral strategies to reduce urinary and colorectal symptoms were performed at each visit. Self-reported adherence to BPMT was assessed at 6, 12, and 24 months. All BPMT interventionists attended centralized in-person training prior to the initiation of the study.

Data collection occurred at baseline, during surgery and hospitalization, and at regular intervals up to 24 months postoperatively with Pelvic Organ Prolapse Quantification (POPQ)[18] evaluations and symptom assessments occurring at 6, 12 and 24 months. BPMT interventionists were masked to surgical randomization. All outcome assessors were masked to both perioperative BPMT and surgical intervention assignment, including research personnel who conducted vaginal examinations and trained telephone interviewers who administered patient reported outcomes from a centralized facility. Participants were masked to the surgical group assignment, and study surgeons were masked to perioperative BPMT group assignment.

Outcomes

Surgical Intervention—The primary outcome for surgery, assessed at 2 years, used a composite outcome measure of surgical "success" or "failure". We defined "success" as the absence of all of the following: (1) descent of the vaginal apex more than one-third into the vaginal canal, (2) anterior or posterior vaginal wall descent beyond the hymen, (3) bothersome vaginal bulge symptoms as indicated by an affirmative response to either "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?" in the Pelvic Floor Distress Inventory (PFDI)[22], and any response other than "not at all" to the question "How much does this bother you?", or (4) retreatment for prolapse by either surgery or pessary. Secondary surgical outcomes included maximum prolapse of each vaginal segment (anterior, posterior and apical); urinary, bowel and prolapse symptoms (PFDI, Incontinence Severity Index[23]); retreatment for prolapse or urinary incontinence; and adverse events.

An independent data and safety monitoring board reviewed trial progress and safety. Investigators classified adverse events as serious/non-serious and expected/unexpected. Serious and expected adverse events were further categorized using the Dindo system.[24]

Behavioral Intervention—Primary outcomes for BPMT were assessed at 6 and 24 months. The primary 6-month outcome, urinary symptoms, was assessed by the Urinary Distress Inventory (UDI) score of the PFDI. The minimum important difference of the UDI is 11 points.[25] The primary 24-month outcomes were 1) prolapse symptoms, assessed by the Pelvic Organ Prolapse Distress Inventory (POPDI) score of the PFDI, and 2) anatomic failure defined by: (a) descent of the vaginal apex more than one-third into the vaginal canal, or (b) anterior or posterior vaginal wall descent beyond the hymen, or (c) retreatment for prolapse. In contrast to the primary outcome of the surgical intervention, the presence of vaginal bulge symptoms was not included in the anatomic failure outcome for the BPMT analysis because it is assessed as a component of the POPDI. Secondary outcomes included maximum prolapse (anterior, posterior and apical vaginal segments); retreatment for urinary incontinence and/or prolapse; urinary, prolapse and bowel symptoms (PFDI)[22]; Incontinence Severity Index[23]; and pelvic floor muscle strength (Brink grading system).[26]

Sample Size

Study investigators estimated *a priori* that a surgical success difference of less than 15% would not change clinical practice and that the sample size should detect a difference of 10%. A sample size of 121 per surgical group would provide 80% power to detect a difference between surgical failure rates of 70% versus 85% using a two-tailed 5% level of significance. 170 women per surgical group would allow 80% power to differentiate between success rates of 70% and 83% using a two-tailed 5% level of significance and also allow 80% power to identify a group difference of 0.3 standard deviations in mean UDI score between BPMT and usual care groups using a two-tailed 5% level of significance. We increased our enrollment goal to 200 per group to allow for a 15% drop out rate. We stopped enrollment at 418 participants (374 randomized) because our early loss to follow-up was lower than expected. Our final sample size of 309 women with primary outcome data was sufficient to provide 80% power to detect a 15% treatment difference (noted *a priori* by the investigators to be clinically relevant) though the final number of participants with 24-month data was lower than expected. The study was not powered to detect interactions between the surgical and behavioral interventions.

Statistical Analysis

The analysis was performed on all participants who underwent randomization for both the BPMT intervention and the surgical intervention, and participants were analyzed in the groups to which they were randomized. Baseline demographic and clinical characteristics were compared between surgical treatment groups and between BPMT treatment assignments using general linear models for continuous outcomes and generalized linear models for categorical outcomes. Baseline models included variables for surgical group, BPMT treatment assignment, and their interaction. For the primary outcome, a p value (two-sided) less than 0.05 was considered statistically significant. Analyses of secondary

outcomes were considered exploratory in nature, and p values and confidence intervals are provided for descriptive purposes only.

Surgical Intervention—Differences between the surgical groups in the primary outcome of surgical success at 24 months and other categorical outcomes were evaluated using generalized linear models with a logit link and terms for surgical group, BPMT treatment assignment, and their interaction, as well as stratification factors for surgeon and concomitant hysterectomy. Because of the large number of surgeons involved in the study (31 surgeons from 9 sites), surgeon was included in the outcome models as a random effect. If the interaction reached statistical significance at the $p<0.05$ level, surgical groups were compared within each BPMT group; otherwise the marginal differences between surgical groups were compared. Similar models were used to compare occurrence of adverse events except that a cumulative logit link was employed for multinomial outcomes. Continuous outcomes were compared using analogous general linear models. For outcomes for which data were available at multiple time points (for example, bothersome vaginal bulge symptoms at 6, 12 and 24 months), a longitudinal extension to the generalized linear model that included terms for time as a categorical variable was used, and tests comparing the surgical groups at each time point were conducted. Longitudinal models additionally included interactions between the BPMT and surgical treatments and time.

For the primary analysis, women with missing anatomic data at the 2-year time point, data from the last available physical examination were used. Women who met failure criteria based on their last exam were considered surgical failures at 2 years; however, those who did not meet failure criteria and had missing data at 2 years were considered missing at 2 years. Missing surgical failure outcomes were multiply imputed and a sensitivity analysis conducted to assess the robustness of the primary analysis results.

Behavioral Intervention—For the primary outcome of UDI score at 6 months, outcomes were imputed using Brown's method for participants who had reported use of medication for lower urinary tract symptoms, stress incontinence surgery including urethral bulking agent injections, neuromodulation, intravesical botulinum toxin injections, or enrollment in a supervised pelvic floor therapy program to address potential biases in the UDI introduced through those added treatments.[27] The imputed UDI score at 6 months was analyzed using a Mann-Whitney-Wilcoxon test. In addition, we used a common linear mixed model using non-imputed data that included terms for BPMT treatment, surgical treatment, and their interaction, as well as clinical site, and terms for time as a categorical variable and the two and three way interactions of time with the treatment variables to evaluate the effect of BPMT treatment on the change from baseline in 1) UDI at 6, 12, and 24 months, and 2) other elements of the PFDI at 6, 12, and 24 months. Two year anatomic outcomes for the behavioral intervention were analyzed using models analogous to those described above for the surgical intervention, but modified to control for site as a fixed effect rather than for hysterectomy and surgeon, reflecting the differences in the stratification factors for the BPMT and surgical randomizations. When the treatment interaction reached statistical significance at the $p<0.05$ level, BPMT groups were compared within each surgical group; otherwise marginal effects of the BPMT treatment groups were compared.

As with the surgical failure outcome, the anatomic failure outcome for the behavioral intervention used data from the last available physical examination for women with missing anatomic data at the 2-year time point. Women who met failure criteria based on their last examination were considered anatomic failures at 2 years; however, those who did not meet failure criteria and had missing data at 2 years were considered missing at 2 years for statistical analysis. In sensitivity analyses, missing anatomic failure outcomes were multiply imputed, as were changes from baseline in UDI scores at 6 months and POPDI subscale scores at 24 months for women who were missing the UDI or POPDI or who underwent stress incontinence or prolapse retreatment, respectively. Sensitivity analyses using the multiply imputed data were conducted to assess the robustness of the original analyses.

RESULTS

Study Populations and Treatment Assignments

The OPTIMAL trial enrolled 418 eligible women and 408 women underwent the behavioral therapy randomization preoperatively. Thirty-four participants withdrew prior to surgery leaving 374 women who were randomized to both the surgical intervention (ULS n=188 vs. SSLF n=186) and behavioral intervention (BPMT n=186 vs. usual care n=188) and were included in this analysis (Figure 1). The groups had similar rates of post-randomization withdrawals at 24 months [ULS 27 (14.4%), SSLF 31 (16.7%), p=0.59 and BPMT 34 (18.3%), usual care 24 (12.8%), p=0.15].

Baseline clinical characteristics were similar between the surgical groups and the behavioral intervention groups with the exception of a greater degree of posterior vaginal prolapse in the SSLF group and a higher median number of vaginal deliveries in the ULS group (Table 1 and eTable 3). We noted significant interaction effects between surgical and BPMT groups for age and BMI; however, within BPMT groups the surgical groups were balanced. There were no BPMT or usual care group differences in surgical intervention; 50% of both groups underwent each surgical study procedure (ULS and SSLF) and all but 3 women in the study population (99%) underwent TVT (eTable 4).

Surgical Intervention Outcomes

At two years, there was no statistically significant difference in surgical success as defined by the composite primary outcome [ULS 59.2% (93/157) versus SSLF 60.5% (92/152), OR 0.9, 95% CI (0.6, 1.5)] between the surgical groups, and no clinically significant differences in any of the 4 primary outcome components (Table 2 a & b). Analysis of the multiply imputed surgical failure outcome was consistent with the primary analysis [ULS 111/188=59.1% vs. SSLF 116/186=62.4%, OR 0.9, 95% CI (0.6, 1.5)]. Overall, 18.0% of women (55/305) developed bothersome vaginal bulge symptoms, 17.5% (54/308) had anterior and/or posterior prolapse beyond the hymen and 5.1% (16/316) underwent retreatment with either a pessary or surgery by two years. An interaction effect between surgical and BPMT groups was noted for the apical descent component of surgical success (Table 2). In women receiving usual care, those in the ULS group were less likely to develop apical descent than those receiving SSLF [ULS 8.6% versus SSLF 20.8%, OR 0.3,

95% CI (0.1, 0.9)]. In women receiving BPMT there was no significant difference in apical descent [ULS 23.0% versus SSLF 12.0%, OR 2.2, 95% CI (0.9, 5.3)].

Surgical groups were not significantly different for most secondary outcome measures including operative variables such as estimated blood loss, time of surgery and duration of hospitalization (eTable 4) and postoperative treatments for prolapse and incontinence (eTable 5). A greater proportion of women in the SSLF group had “any” or “bothersome” vaginal bulge symptoms at 6 and 12 months as compared to the women in the ULS group (eTable 6a). By 24 months, these proportions were similar without clinically relevant differences.

The most common perioperative adverse event was bladder perforation associated with TVT placement; the most common long-term complication was presence of vaginal granulation tissue (Table 3). The proportion of women who experienced serious adverse events during the study was not significantly different between surgical groups [ULS 16.5% vs. SSLF 16.7%, OR 0.9, 95% CI (0.5, 1.6)]. The rate of neurologic pain requiring intervention was higher in the SSLF group [ULS 6.9% vs. SSLF 12.4%, OR 0.5, 95% CI (0.2, 1.0), p=0.049] and persisted to the 4–6 week postoperative visit in more participants [ULS n=1, (0.5%) versus SSLF, n=8 (4.3%)]. Ureteral obstruction was recognized and successfully managed intraoperatively in 5 (3.2%) in the ULS group. One patient’s ureteral injury was detected post-operatively after ULS (0.5%). Ureteral obstruction was not seen in the SSLF group.

Behavioral Intervention Outcomes

There were no significant differences between BPMT and usual perioperative care in the 6-month and 24-month patient-reported primary outcomes (Table 4). After imputation by Brown’s method, the median UDI score at 6 months was 12.7 in both the BPMT and usual care groups, and a test for differences in distributions between groups was not significant (p=0.61). Using non-imputed data, the adjusted mean change from baseline UDI total score at 6 months was −94.6 in the BPMT group versus −87.9 in the usual care group (95% CI for difference −19.7 to 6.2; p=0.31); these findings remained stable through 24 months. Results based on the multiply imputed change from baseline UDI at 6 months were similar [−94.5 in BPMT versus −87.0 in usual care, 95% CI for difference (−19.7, 4.9), p=0.24]. Compared to baseline, the decrease in POPDI score at 24 months was not significantly different between groups [−73.3 in BPMT versus −65.2 in usual care, 95% CI for difference (−22.1, 6.1), p=0.26]. Results from the multiply imputed POPDI scores were consistent [−74.6 in BPMT versus −65.5 in usual care, 95% CI for difference (−24.6, 6.6), p=0.25]. There were no significant group differences at other time points for PFDI subscales (Table 4). To examine potential effect modification or confounding of outcomes by baseline pelvic floor muscle strength, these analyses were repeated including terms for baseline Brink score and Brink score by BPMT treatment assignment interaction with no substantive change in results.

There was a significant interaction (effect modification) between the behavioral and surgical intervention groups for the primary anatomic failure outcome at 24 months; however, failure was not significantly different between behavioral groups within each surgical treatment [ULS group: BPMT 26/78 (33.3%) versus usual care 22/86 (25.6%), OR 1.8, 95% CI (0.9, 3.8); SSLF group: BPMT 19/77 (24.7%) versus usual care 27/80 (33.8%), OR 0.6, 95% CI

(0.3, 1.2)] (Table 2 a & b). Results based on the multiply-imputed anatomic failure outcome were consistent [ULS group: BPMT 32/91 (34.9%) versus usual care 24/97 (24.5%), OR 1.9, 95% CI (0.9, 3.9); SSLF group: BPMT 23/95 (24.2%) versus usual care 29/91 (32.1%), OR 0.6, 95% CI (0.3, 1.2)]. We did not detect group differences in the proportion of women with an anatomic failure due to anterior or posterior prolapse, or retreatment (Table 2 & eTables 5, 6b, 6c). The anterior vagina was the most likely vaginal compartment to prolapse beyond the hymen; proportions were not significantly different between groups [BPMT 14.1% versus usual care 15.1%, OR 0.9, 95% CI 0.5, 1.8] (Table 2). As described previously, there was a significant interaction between the BPMT and surgical groups such that women in the ULS group randomized to BPMT were more likely to have apical descent more than one-third of total vaginal length (Table 2). Apical descent in women in women randomized to SSLF was not different between behavioral groups.

No differences were noted between BPMT and usual care groups for secondary patient reported outcome measures including retreatment for incontinence [OR 1.4; 95% CI (0.8, 2.3)] or prolapse [OR 2.5; 95% CI (0.8, 7.6)] (eTables 5 and 7). Baseline pelvic floor muscle strength was moderately strong, with a mean score of 8 on the Brink score (Brink range 3–12). No group differences in change in pelvic floor strength were noted from baseline at 6 or 24 months. At 24 months, mean Brink scores were 8.2 and 8.0 in BPMT and usual care groups respectively (p=0.27). Self-reported performance of pelvic muscle exercises in the BPMT group was 93.4% at 6 months and 81.4% at 24 months. In the usual care group, 8 of 186 women (4.3%) received supervised BPMT outside of the study by 24 months.

DISCUSSION

In women with apical vaginal prolapse (uterine or post-hysterectomy vault) and stress urinary incontinence, the OPTIMAL trial found that neither of two common apical transvaginal prolapse repair procedures, ULS and SSLF, was superior to the other. In addition, a multi-component, perioperative BPMT program did not improve urinary or prolapse outcomes and is likely unnecessary as a routine aspect of perioperative care.

Our success rates for the surgical intervention, defined by a rigorous composite definition for treatment success that included anatomic results, patient reported symptoms, and retreatment, were lower than the 70–90% success rates generally reported in the literature for these procedures. This is consistent with other multi-center surgical trials where treatment success rates were typically lower when defined by composite outcomes.[28–30] However, retreatment rates remained low at 5%. Additionally, the use of masked POPQ examiners[31] and strict anatomic criteria for apical descent likely contributed to these lower success rates. In the absence of high quality clinical trials, surgeons have relied primarily on case series reporting rates of anterior vaginal wall prolapse after SSLF as high as 40%,[32,33] and have attributed these high rates to posterior deviation of the vaginal apex. Our findings showed that the proportion of women with recurrent anterior (ULS 15.5% vs. SSLF 13.7%) or posterior prolapse (ULS 4.5% vs. SSLF 7.2%) beyond the hymen were not significantly different between treatment groups, highlighting the importance of these Level 1 data. One unexpected finding was that women randomized to ULS had greater apical descent if they received perioperative BPMT rather than usual care; this was not seen in those randomized

to SSLF. It is unclear why BPMT would have this differential effect but one possible explanation is the difference in orientation of the vagina after the two suspension procedures.

The low rates of serious adverse events seen in both groups are consistent with the clinical experience of the safety of native tissue vaginal reconstructive surgery. Fewer than one in five women experienced a serious adverse event over the two-year follow-up, with <5% directly related to the index surgery. As expected based on anatomical differences in surgical approach, we observed more ureteral obstructions occurring in ULS (3.7%) than SSLF (0%). These rates are within previously reported ureteral injury rates, which range from 1 to 11% following ULS.[34] Notably, all intra-operatively identified ureteral obstructions were adequately treated during the index surgery by removing the obstructing sutures or stent placement. This study confirms the findings of previous case series suggesting that SSLF is more likely to result in acute neurologic pain, particularly buttock pain thought due to gluteal nerve entrapment.[32,35] While the majority had resolution of the pain by 4–6 weeks postoperatively, persistent pain occurred in 4.3% after SSLF highlighting the need to counsel patients about this risk preoperatively.

The findings of our perioperative BPMT intervention are consistent with a pilot study (n=51) by Frawley and colleagues, who found no significant effects for perioperative physiotherapist-supervised pelvic floor muscle training for women undergoing vaginal surgery for prolapse or hysterectomy.[36] Although their intervention included more sessions (8) over a longer period of time (12 months), their study also did not detect significant group differences 12 months post-surgery on urinary questionnaires, bladder diary or pad test.

In contrast, Jarvis and colleagues reported that perioperative physiotherapy improved outcomes 3 months after surgery for prolapse and/or stress incontinence with significant group differences in urinary symptoms, quality of life, pelvic floor muscle strength, and voiding frequency. Despite the similarities of the OPTIMAL trial to that trial, several relevant differences include a smaller sample (n=60) and different outcomes at an earlier time point (3 months).[37] The training of BPMT interventionists also differed. Similar to Frawley, the Jarvis study intervention was implemented by established interventional physiotherapists, whereas our trial provided centralized training for clinicians with varying degrees of BPMT experience. Nonetheless, only those certified based on rigorous in-person testing were allowed to participate as BPMT interventionists in the OPTIMAL trial.[17] Additionally, the broad range of experience of the OPTIMAL interventionists increases the generalizability our findings.

The outcomes in this study should not be extrapolated to women who do not match our eligibility criteria, including women who do not undergo concomitant mid-urethral sling for treatment of stress incontinence. Our participants underwent both prolapse and stress incontinence procedures with high efficacy rates, which may have overshadowed any additional improvement provided by a perioperative BPMT intervention. These findings should also not be extrapolated to women undergoing transvaginal mesh or abdominal mesh augmented prolapse repairs.

Our conclusions benefit from a robust study design, standardized anatomic and functional outcomes with validated patient reported outcomes, and patients and outcome assessors masked to the surgical intervention assignment. Our findings are further strengthened by the multi-center, multi-surgeon, randomized design, with standardization of surgical techniques and the high rate of participant retention. In addition, perioperative BPMT program intervention was individualized using a standard protocol and consisted of multiple components, including strategies for stress and urgency incontinence, recommendations for normal voiding and defecation techniques, and ongoing reinforcement of functional bracing (pelvic floor contraction during lifting and physical activity) thought to protect the surgical repair and the pelvic floor long-term.

This study provides evidence for patients and their surgeons about the benefits, risks and complications of two widely used native tissue vaginal approaches for apical prolapse, as well as the role of perioperative BPMT. While our results do not support routinely offering perioperative BPMT to women undergoing vaginal surgery for prolapse and stress urinary incontinence, previous evidence supports offering individualized treatment, including behavioral or physical therapy, to those who report new or unresolved pelvic floor symptoms. Our surgical outcomes inform preoperative discussions that include a patient's preferences for anatomic and subjective outcomes as well as consideration of likely and possible adverse events. While variability in surgical recommendations for vaginal prolapse repair are likely to persist due to individualized patient characteristics, our data provide a metric against which other vaginal procedures, including those which use synthetic or biologic mesh, can be assessed.

Conclusions

In women undergoing vaginal surgery for pelvic organ prolapse and stress urinary incontinence, neither ULS nor SSLF was significantly superior to the other for anatomic, functional, or adverse event outcomes two years after surgery. Perioperative BPMT in these women did not improve urinary symptoms at 6 months or prolapse outcomes two years after surgery.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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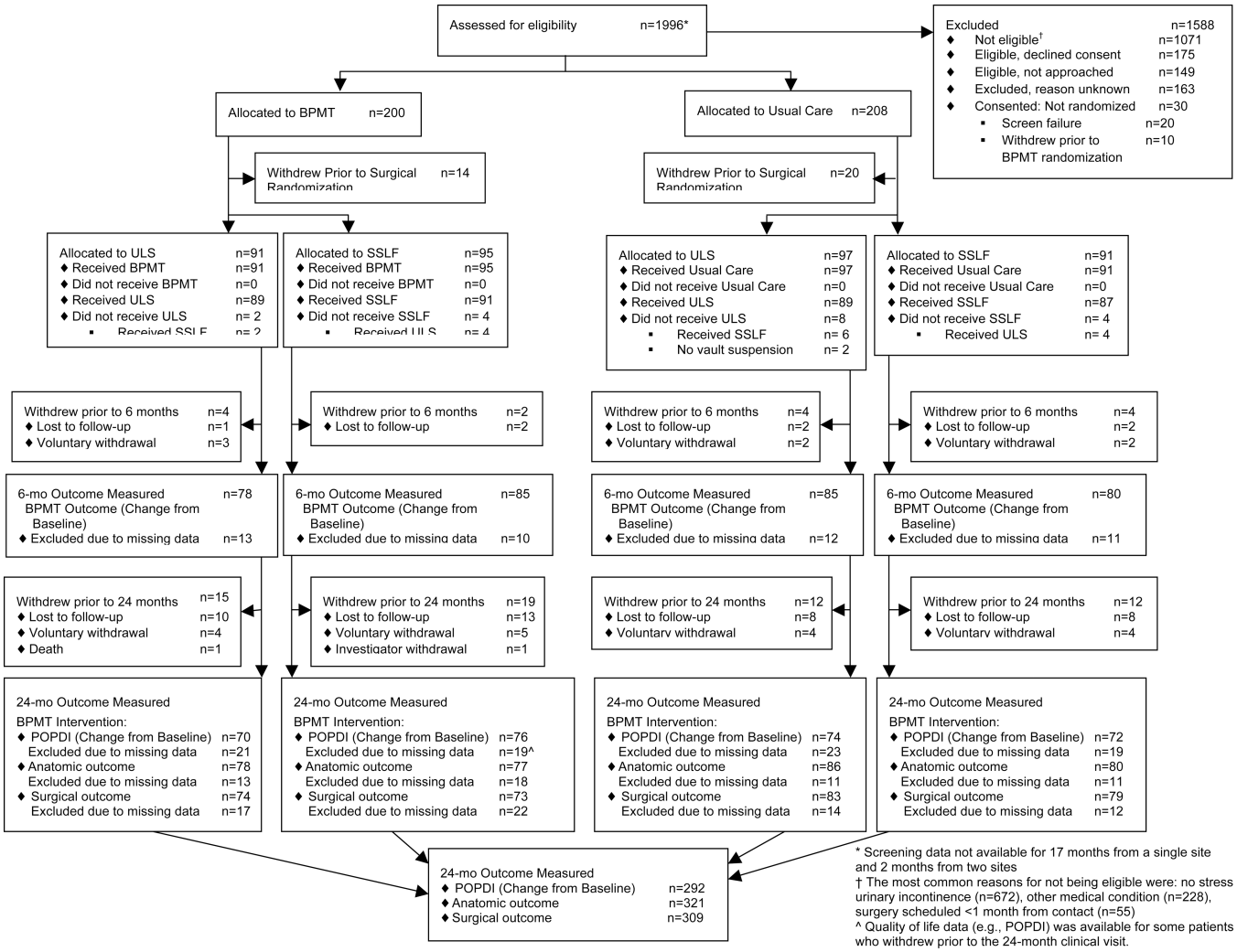

Figure 1.
Optimal Trial Enrollment, Randomization and Assessment.

Table 1

Demographics and Baseline Characteristics

Variable	BPMT Group Comparisons			Surgical Group Comparisons		
	Treatment Group		*P* value*	Treatment Group		*P* value*
	BPMT N=186	Usual Care N=188		Uterosacral Ligament Suspension N=188	Sacrospinous Ligament Fixation N=186	
Age, yrs.						
Mean (SD)	57.5 (10.9)	56.9 (10.9)		57.3 (10.8)	57.2 (11.0)	
Min, Max	29.0, 80.0	31.0, 80.0		29.0, 80.0	32.0, 80.0	
Age, n (%)			N/A – Significant BPMT by Surgery interaction (*P* value for interaction = 0.04)			N/A – Significant BPMT by Surgery interaction (*P* value for interaction = 0.04)
>=29 and <=40	15 (8.1%)	10 (5.3%)		10 (5.3%)	15 (8.1%)	
>40 and <=50	40 (21.5%)	45 (23.9%)		45 (23.9%)	40 (21.5%)	
>50 and <=60	59 (31.7%)	68 (36.2%)		66 (35.1%)	61 (32.8%)	
>60 and <=70	49 (26.3%)	40 (21.3%)		42 (22.3%)	47 (25.3%)	
>70 and <=80	23 (12.4%)	25 (13.3%)		25 (13.3%)	23 (12.4%)	
Race, n (%)			0.45			0.94
White/Caucasian	154 (82.8%)	161 (85.6%)		158 (84.0%)	157 (84.4%)	
Black/African American	15 (8.1%)	7 (3.7%)		12 (6.4%)	10 (5.4%)	
Asian	1 (0.5%)	3 (1.6%)		0 (0.0%)	4 (2.2%)	
American Indian/Alaskan	1 (0.5%)	1 (0.5%)		0 (0.0%)	2 (1.1%)	
Other	15 (8.1%)	16 (8.5%)		18 (9.6%)	13 (7.0%)	
Ethnicity, n (%)			0.80			0.39
Hispanic	38 (20.4%)	37 (19.7%)		41 (21.8%)	34 (18.3%)	
Non-Hispanic	148 (79.6%)	151 (80.3%)		147 (78.2%)	152 (81.7%)	
Insurance						
Private/HMO	125 (67.2%)	126 (67.0%)	0.96	128 (68.1%)	123 (66.1%)	0.68
Medicaid/Medicare	56 (30.1%)	53 (28.2%)	0.68	56 (29.8%)	53 (28.5%)	0.78
Self-Pay	3 (1.6%)	3 (1.6%)	0.99	3 (1.6%)	3 (1.6%)	0.99

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Variable	BPMT Group Comparisons			Surgical Group Comparisons		
	Treatment Group		*P* value*	Treatment Group		*P* value*
	BPMT N=186	Usual Care N=188		Uterosacral Ligament Suspension N=188	Sacrospinous Ligament Fixation N=186	
Other	33 (17.7%)	39 (20.7%)	0.47	37 (19.7%)	35 (18.8%)	0.89
Vaginal deliveries, n			0.18			0.01
Median	3.0	3.0		3.0	2.0	
Min, Max	0.0, 15.0	0.0, 12.0		0.0, 15.0	0.0, 12.0	
Cesarean deliveries, n			0.18			0.01
Median	0.0	0.0		0.0	0.0	
Min, Max	0.0, 4.0	0.0, 2.0		0.0, 4.0	0.0, 4.0	
Menstrual status, n (%)			0.60			0.99
Pre-menopausal	50 (26.9%)	56 (29.8%)		54 (28.7%)	52 (28.0%)	
Post-menopausal	123 (66.1%)	123 (65.4%)		123 (65.4%)	123 (66.1%)	
Not sure	13 (7.0%)	9 (4.8%)		11 (5.9%)	11 (5.9%)	
Currently using estrogen replacement therapy, n (%)						
Oral/Patch	22 (11.8%)	24 (12.8%)	0.86	20 (10.6%)	26 (14.0%)	0.34
Vaginal	42 (22.6%)	46 (24.5%)	0.66	49 (26.1%)	39 (21.0%)	0.24
Current smoker, n (%)	19 (10.2%)	14 (7.4%)	0.36	14 (7.4%)	19 (10.2%)	0.36
Diabetes mellitus, n (%)	27 (14.9%)	17 (9.2%)	0.10	24 (12.8%)	20 (11.2%)	0.65
Connective tissue disease (SLE, Marfans, Sjogrens, Scleroderma), n (%)	2 (1.1%)	3 (1.6%)	N/A - LN	4 (2.2%)	1 (0.5%)	N/A – LN
Prior hysterectomy, n (%)	45 (24.2%)	55 (29.3%)	0.27	48 (25.5%)	52 (28.0%)	0.62
Prior stress urinary incontinence surgery, n (%)	6 (3.2%)	7 (3.7%)	0.74	7 (3.7%)	6 (3.2%)	0.74
Prior pelvic organ prolapse surgery, n (%)	9 (4.8%)	17 (9.0%)	0.13	9 (4.8%)	17 (9.1%)	0.11

Variable	BPMT Group Comparisons			Surgical Group Comparisons		
	Treatment Group		*P* value*	Treatment Group		*P* value*
	BPMT N=186	Usual Care N=188		Uterosacral Ligament Suspension N=188	Sacrospinous Ligament Fixation N=186	
Body mass index, kg/m^2			(*P* value for interaction = 0.048)			(*P* value for interaction = 0.048)
Mean (SD)	29.3 (5.6)	28.4 (5.3)		28.7 (5.2)	29.0 (5.7)	
Min, Max	19.3, 49.8	19.7, 46.3		19.3, 46.3	19.6, 49.8	
Pelvic Organ Prolapse Quantification (POPQ) Stage,* n (%)	1	2	0.93			0.50
2	72 (38.7%)	71 (37.8%)		70 (37.2%)	73 (39.2%)	
3	105 (56.5%)	108 (57.4%)		111 (59.0%)	102 (54.8%)	
4	9 (4.8%)	9 (4.8%)		7 (3.7%)	11 (5.9%)	
Regularly perform pelvic floor muscle exercises, N (%)	45 (24.3%)	35 (18.8%)	0.21	38 (20.4%)	42 (22.7%)	0.68
Prior supervised pelvic floor muscle exercise program, N (%)	10 (5.4%)	4 (2.2%)	0.11	7 (3.8%)	7 (3.8%)	0.60
Vaginal bulge symptoms, n, (%)						
Any	186 (100.0%)	188 (100.0%)	N/A - LN	188 (100.0%)	186 (100.0%)	N/A - LN
Bothersome	167 (93.8%)	163 (92.6%)	0.65	164 (93.7%)	166 (92.7%)	0.71
Prolapse beyond the hymen, n (%)						
Anterior (POPQ Aa or Ba >0)	126 (67.7%)	144 (76.6%)	0.06	142 (75.5%)	128 (68.8%)	0.15
Posterior (POPQ Ap or Bp>0)	38 (20.4%)	35 (18.6%)	0.82	26 (13.8%)	47 (25.3%)	0.01
Apical (POPQ C >0)	56 (30.3%)	59 (31.4%)	0.81	55 (29.3%)	60 (32.4%)	0.51
Apical descent greater than or equal to ½ of total vaginal length (n, %) (POPQ C>=−1/2*TVL)	182 (98.4%)	186 (98.9%)	0.70	185 (98.4%)	183 (98.9%)	0.72
Most distal point of vaginal segment, mean cm (SD)#						
Anterior	2.1 (2.3)	2.2 (2.1)	0.84	2.1 (2.1)	2.2 (2.4)	0.93

Variable	BPMT Group Comparisons			Surgical Group Comparisons		
	Treatment Group		*P* value*	Treatment Group		*P* value*
	BPMT N=186	Usual Care N=188		Uterosacral Ligament Suspension N=188	Sacrospinous Ligament Fixation N=186	
Posterior	0.6 (2.8)	0.5 (2.7)	0.70	0.2 (2.5)	0.8 (2.9)	0.04
Apical	−0.8 (3.5)	−1.0 (3.5)	0.58	−1.0 (3.3)	−0.7 (3.7)	0.38
Maximum descent of any segment, mean cm, (SD)#	2.3 (2.2)	2.3 (2.1)	0.90	2.2 (2.0)	2.4 (2.2)	0.53
POPQ value, median cm (minimum, maximum)##						
Aa	1.0 (−3.0, 3.0)	1.0 (−2.0, 3.0)		1.0 (−2.0, 3.0)	1.0 (−3.0, 3.0)	
Ba	2.0 (−2.0, 11.0)	2.0 (−2.0, 11.0)		2.0 (−2.0, 11.0)	2.0 (−2.0, 10.0)	
C	−2.0 (−6.0, 11.0)	−2.0 (−6.0, 11.0)		−2.0 (−5.0, 11.0)	−2.0 (−6.0, 10.0)	
Ap	−1.3 (−3.0, 3.0)	−1.0 (−3.0, 3.0)		−2.0 (−3.0, 3.0)	−1.0 (−3.0, 3.0)	
Bp	−1.0 (−3.0, 11.0)	−1.0 (−3.0, 11.0)		−1.0 (−3.0, 11.0)	−1.0 (−3.0, 10.0)	
GH	4.5 (2.0, 10.0)	4.5 (2.0, 8.0)		4.5 (2.0, 8.0)	4.5 (2.0, 10.0)	
PB	3.0 (0.0, 6.0)	3.0 (1.0, 7.0)		3.0 (1.0, 6.0)	3.0 (0.0, 7.0)	
TVL	9.5 (5.5, 12.0)	9.5 (3.0, 12.0)		9.5 (3.0, 12.0)	10.0 (5.5, 12.0)	

BPMT, Behavioral and Pelvic Floor Muscle Therapy; POPQ, Pelvic Organ Prolapse Quantification system N/A – LN = The *P* value is not shown due to low Ns leading to low reliability of test.

*Pelvic Organ Prolapse Quantification (POPQ) Stages: 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 is less than totally everted; Stage 4 - The vagina is everted to within 2 cm of its length.

#Most distal point of each compartment and overall are measured in cm relative to the hymen during maximum strain with descent to the hymen = 0, descent proximal to the hymen as a negative value and descent distal to the hymen as positive value using the POPQ system. The most distal point of the apical segment is equal to POPQ point C; Most distal point of the anterior segment = POPQ point Ba if Ba ≥C or is = C if Ba<C; most distal point of posterior segment = POPQ point Bp if Bp ≥C or is = C if Bp<C.

##POPQ values provided for descriptive purposes only. In the POPQ system, the positions of C, Ba, and Bp are measured at the most dependent location (the point of greatest prolapse) of the apex, anterior vaginal wall and posterior vaginal wall respectively during a straining. Values are measured in cm and are negative if above the hymen, and positive if below the hymen. TVL (total vaginal length), GH (genital hiatus) and PB (perineal body) are measured as positive values.

NOTE: “N/A – Significant BPMT*Surgery interaction” represents an effect that was significant in the model at the .05 alpha level. In these cases, the adjusted means and test results are reported below within BPMT and Usual care groups.

Mean Age, years: ULS Group: BPMT, 58.7 vs. Usual care, 55.8, p=0.07; SSLF Group: BPMT, 56.3 vs. Usual care, 58.1, p=0.25

Mean BMI, kg/m^2: ULS Group: BPMT, 28.6 vs. Usual care, 28.8, p=0.77; SSLF Group: BPMT, 30.0 vs. Usual care, 28.0, p=0.01

Mean Age, years: BPMT group, ULS, 55.8 vs. SSLF, 58.1, p=0.12; usual care group, ULS, 58.7 vs SSLF, 56.3, p=0.15

Mean BMI, kg/m^2: BPMT group, ULS, 28.8 vs. SSLF, 28.0, p=0.08; usual care group, ULS 28.6 vs SSLF, 30.0, p=0.29

NOTE: The *P* value for race tests White vs. all other races due to low sample size in minority categories.

NOTE: *P* values correspond to tests between means, even for characteristics showing medians.

Table 2

a. Pelvic Organ Prolapse Outcomes at 24 months

Variable	Surgical Group Comparisons				BPMT Group Comparison			
	Treatment Group		Surgical Adjusted OR (95% CI)	*P* value	Treatment Group		BPMT Adjusted OR (95% CI)	*P* value
	ULS N=188	SSLF N=186			BPMT N=186	Usual Care N=188		
Surgical Success	93/157 (59.2%)	92/152 (60.5%)	0.9 (0.6, 1.5)	0.75				
Anatomic Failure					45/155 (29.0%)	49/166 (29.5%)	See Table 2b	
Vaginal Bulge Symptoms*								
Bothersome	25/151 (16.6%)	30/154 (19.5%)	0.8 (0.5, 1.5)	0.49	27/151 (17.9%)	28/154 (18.2%)	1.0 (0.5, 1.9)	1.00
Any	29/151 (19.2%)	32/154 (20.8%)	0.9 (0.5, 1.6)	0.70	31/151 (20.5%)	30/154 (19.5%)	1.1 (0.6, 2.0)	0.75
Apical Descent >1/3rd of total vaginal length (POPQ point C>-2/3*TVL)	24/155 (15.5%)	25/152 (16.4%)	See Table 2b		26/149 (17.4%)	23/158 (14.6%)	See Table 2b	
Prolapse Beyond the Hymen*								
Anterior (POPQ Aa or Ba >0)	24/155 (15.5%)	21/153 (13.7%)	1.2 (0.6, 2.2)	0.65	21/149 (14.1%)	24/159 (15.1%)	0.9 (0.5, 1.8)	0.79
Posterior (POPQ Ap or Bp >0)	7/155 (4.5%)	11/153 (7.2%)	0.6 (0.3, 1.3)	0.21	7/149 (4.7%)	11/159 (6.9%)	0.6 (0.2, 1.5)	0.24
Apical (POPQ C >0)	7/155 (4.5%)	9/152 (5.9%)	0.9 (0.3, 2.5)	0.86	6/149 (4.0%)	10/158 (6.3%)	0.6 (0.2, 1.8)	0.37
Retreatment for POP								
Surgery	5/161 (3.1%)	4/155 (2.6%)	1.4 (0.3, 6.0)	0.66	4/152 (2.6%)	5/164 (3.0%)	0.7 (0.2, 3.3)	0.70
Pessary	5/161 (3.1%)	5/155 (3.2%)	1.0 (0.2, 4.7)	0.97	8/152 (5.3%)	2/164 (1.2%)	4.4 (0.9, 21.6)	0.07
Either Surgery or Pessary	8/161 (5.0%)	8/155 (5.2%)	0.9 (0.3, 2.6)	0.81	11/152 (7.2%)	5/164 (3.0%)	2.5 (0.8, 7.6)	0.11

	Treatment Group		Adjusted Mean Treatment Difference (95% CI)	*P* value	Treatment Group		Adjusted Mean Treatment Difference (95% CI)	*P* value
	ULS N=188	SSLF N=186			BPMT N=186	Usual Care N=188		
Most distal point of vaginal segment adjusted mean cm (SE)[#]:								
Anterior	−0.5 (0.2)	−0.4 (0.2)	−0.1 (−0.6, 0.4)	0.73	−0.5 (0.2)	−0.4 (0.2)	−0.2 (−0.6, 0.3)	0.53
Posterior	−1.6 (0.2)	−1.6 (0.2)	−0.0 (−0.5, 0.5)	0.98	−1.6 (0.2)	−1.6 (0.2)	−0.1 (−0.5, 0.4)	0.81
Apical	See Table 2b				See Table 2b			
Maximum descent of any segment adjusted mean cm, (SE)	−0.2 (0.2)	−0.2 (0.2)	−0.1 (−0.5, 0.4)	0.78	−0.3 (0.2)	−0.2 (0.2)	−0.1 (−0.6, 0.4)	0.63

b. Within-Group Comparisons for Significant Interactions Between Surgical and Behavioral Intervention Groups

Variable	Comparisons within ULS Group				Comparisons within SSLF Group			
	Treatment Group		Adjusted OR (95% CI)	*P* value	Treatment Group		Adjusted OR (95% CI)	*P* value
	BPMT N=91	Usual Care N=97			BPMT N=95	Usual Care N=91		
Anatomic Failure (interaction *P* value 0.03)	26/78 (33.3%)	22/86 (25.6%)	1.8 (0.9, 3.8)	0.10	19/77 (24.7%)	27.80 (33.8%)	0.6 (0.3, 1.2)	0.15
Apical Descent >1/3rd of total vaginal length (POPQ point C>-2/3*TVL) (interaction *P* value 0.005)	17/74 (23.0%)	7/81 (8.6%)	3.8 (1.4, 10.2)	0.01	9/75 (12.0%)	16/77 (20.8%)	0.5 (0.2, 1.2)	0.10
	Comparisons within ULS Group				**Comparisons within SSLF Group**			
	Treatment Group		Adjusted OR (95% CI)	*P* value	Treatment Group		Adjusted OR (95% CI)	*P* value
	BPMT N=91	Usual Care N=97			BPMT N=95	Usual Care N=91		
Most distal point of vaginal segment (adjusted mean, SE)[#] Apical (interaction *P* value 0.01)	−6.1 (3.3)	−6.0 (2.7)	0.6 (−0.4, 1.6)	0.26	−5.6 (2.4)	−5.2 (3.7)	−1.0 (−2.0, 0.0)	0.06
	Comparisons within ULS Group				**Comparisons within SSLF Group**			
	Treatment Group		Adjusted OR (95% CI)	*P* value	Treatment Group		Adjusted OR (95% CI)	*P* value
	BPMT N=91	Usual Care N=97			BPMT N=95	Usual Care N=91		
Apical Descent >1/3rd of total vaginal length (POPQ point C>-2/3*TVL) (interaction *P* value 0.005)	17/74 (23.0%)	9/75 (12.0%)	2.2 (0.9, 5.3)	0.08	7/81 (8.6%)	16/77 (20.8%)	0.3 (0.1, 0.9)	0.03
	Comparisons within ULS Group				**Comparisons within SSLF Group**			
	Treatment Group		Adjusted OR (95% CI)	*P* value	Treatment Group		Adjusted OR (95% CI)	*P* value
	BPMT N=91	Usual Care N=97			BPMT N=95	Usual Care N=91		

Most distal point of vaginal segment (adjusted mean, SE)[#] Apical (interaction *P* value 0.03)	−5.5 (0.4)	−6.2 (0.4)	0.7 (−0.4, 1.7)	0.22	−6.0 (0.4)	−5.3 (0.4)	−0.8 (−1.8, 0.3)	0.14

OR=Odds Ratio; CI=Confidence Interval; POPQ=Pelvic Organ Prolapse Quantification, BPMT= Behavioral and Pelvic Floor Muscle Therapy; ULS=Uterosacral Ligament Suspension; SSLF=Sacrospinous Ligament Fixation; SE=Standard Error of Adjusted Mean.

[*] The three-way interaction between time point and the two treatments is excluded from the models for vaginal bulge bymptoms and posterior prolapse beyond the hymen due to model convergence issues. Hysterectomy was excluded from the vaginal bulge symptoms Model due to convergence issues.

[#] Most distal point of each compartment and overall are measured in cm relative to the hymen during maximum strain with descent to the hymen = 0, descent proximal to the hymen as a negative value and descent distal to the hymen as positive value using the POPQ system. The most distal point of the apical segment is equal to POPQ point C; Most distal point of the anterior segment = POPQ point Ba if Ba ≥C or is = C if Ba<C; most distal point of posterior segment = POPQ point Bp if Bp ≥C or is = C if Bp<C.

Table 3

Adverse Events Related to the Surgical Outcome

Variable	Treatment Group		Adjusted OR* (95% CI)	*P* value*
	Uterosacral Ligament Suspension N=188	Sacrospinous Ligament Fixation N=186		
Participants with any Adverse Event (AE), n (%)	140 (74.5%)	142 (76.3%)	0.9 (0.6, 1.4)	0.65
Serious AE, n (%)	31 (16.5%)	31 (16.7%)	0.9 (0.5, 1.6)	0.83
Expected AE, n (%)	130 (69.1%)	130 (69.9%)	0.9 (0.6, 1.5)	0.80
Perioperative Adverse Events (Surgery through 4–6 week postoperatively) – n (%)				
Participants with:				
Bladder injury	22 (11.7%)	18 (9.7%)	1.2 (0.6, 2.4)	0.60
During mid-urethral sling	18 (9.6%)	18 (9.7%)	1.0 (0.5, 2.0)	1.00
Other	4 (2.1%)	0 (0.0%)		N/A - LR
Intraoperative ureteral obstruction	6 (3.2%)	0 (0.0%)		N/A - LR
Treatment:				
Suture removed intra-operatively	5 (2.7%)	0 (0.0%)		N/A - LR
Stent placement	1 (0.5%)	0 (0.0%)		N/A - LR
Additional Procedure	0 (0.0%)	0 (0.0%)		N/A - LR
Ureteral injury – delayed recognition*	1 (0.5%)	0 (0.0%)		N/A - LR
Urethral injury	0 (0.0%)	0 (0.0%)		N/A - LR
Rectal injury	0 (0.0%)	1 (0.5%)		N/A - LR
Major vascular injury	0 (0.0%)	0 (0.0%)		N/A - LR
Blood transfusion	7 (3.7%)	4 (2.2%)	1.9 (0.5, 7.8)	0.38
Neurologic pain requiring treatment**	13 (6.9%)	23 (12.4%)	0.5 (0.2, 1.0)	0.049
Treatment:				
Narcotic pain medication	10 (5.3%)	18 (9.7%)		
Nerve block	0 (0.0%)	2 (1.1%)		
Physical therapy	2 (1.1%)	3 (1.6%)		
Other medication	8 (4.3%)	13 (7.0%)		
Surgical (return to operating for suture removal)	0 (0.0%)	3 (1.6%)		
Long-term complications n (%)				

Variable	Treatment Group		Adjusted OR* (95% CI)	*P* value*
	Uterosacral Ligament Suspension N=188	Sacrospinous Ligament Fixation N=186		
Participants with:				
Vaginal granulation tissue at 6 to 24 months***	36 (19.1%)	26 (14.0%)	1.5 (0.8, 2.6)	0.18
Mesh erosion/exposure at 4 weeks to 24 months***	3 (1.6%)	1 (0.5%)		N/A - LR
Suture exposure at 6 to 24 months***	29 (15.4%)	32 (17.2%)	0.9 (0.5, 1.5)	0.60
Severity (Dindo Scores) for Expected Adverse Events n (%)				
Participants with Expected AE severity (most severe per participant), n (%)				
No such events	30 (16.0%)	22 (11.8%)	N/A	0.58
I	29 (15.4%)	38 (20.4%)		
II	74 (39.4%)	74 (39.8%)		
III	33 (17.6%)	24 (12.9%)		
IV	1 (0.5%)	0 (0.0%)		
V	0 (0.0%)	0 (0.0%)		
Summary of Serious Adverse Events				
Participants with any SAE	31 (16.5%)	31 (16.7%)	0.9 (0.5, 1.6)	0.83
Number of SAEs	40	44		
Dindo Classification:			N/A	0.75
No such events	157 (83.5%)	155 (83.3%)		
I	3 (1.6%)	2 (1.1%)		
II	11 (5.9%)	11 (5.9%)		
III	15 (8.0%)	17 (9.1%)		
IV	1 (0.5%)	1 (0.5%)		
V	1 (0.5%)#	0 (0.0%)		
Participants with SAE by relationship to study				
No such events	157 (83.5%)	155 (83.3%)	N/A	0.74
Not assessable	2 (1.1%)	0 (0.0%)		

Variable	Treatment Group		Adjusted OR* (95% CI)	*P* value*
	Uterosacral Ligament Suspension N=188	Sacrospinous Ligament Fixation N=186		
Unlikely	24 (12.8%)	22 (11.8%)		
Likely	5 (2.7%)	9 (4.8%)		

N/A = Not applicable; OR = Odds Ratio; CI = Confidence Interval.
N/A – LR = The Adjusted OR and *P* value isn't shown due to reliability of test.

* Not identified during surgical procedure.

** Defined a priori as acute-onset pain involving the buttock, groin and/or lower extremity, usually unilateral, occurring on the side or sides where vault suspension stitches have been placed and within one week of the index surgery requiring an alteration of routine postoperative care (e.g., nerve block, physical therapy, return to OR for suture removal, addition of medications used to treat neuropathic pain such as anticonvulsants or tricyclic anti-depressants, or the increase or persistence of narcotic pain medication use beyond 14 days after surgery).

*** Not mutually exclusive. Location and need for or type of treatment not collected. Mesh erosion excludes from the denominator patients who did not receive TVT at surgery.

Patient death not attributable to study surgery.

Severity grade determined by a modified version of the Dindo classification system,[24] which is based on the level of therapy required to treat an event.

Grade		Definition
I		Any deviation from the normal intraoperative or postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions
		Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside
II		Requiring pharmacological treatment with drugs other than such allowed for grade I complications.
	IIa	Oral administration of drugs other than such allowed for grade I, including antibiotics for wound or bladder infections
	IIb	IV administration of drugs other than such allowed for grade I, including antibiotics; blood transfusions and total parenteral nutrition are also included
III		Requiring surgical, endoscopic or radiological intervention
	IIIo	Additional surgical measures required during OPTIMAL procedure
	IIIa	Intervention not under general anesthesia
	IIIb	Intervention under general anesthesia
IV		Life-threatening complication (including CNS complications)* requiring IC/ICU management
	IVa	Single organ dysfunction (including dialysis)
	IVb	Multiorgan dysfunction
V		Death of a patient
Suffix "d"		If the patient suffers from a complication at the time of discharge, the suffix "d" (for "disability") is added to the respective grade of complication. This label indicates the need for a follow-up to fully evaluate the complication.

* Brain hemorrhage, ischemic stroke, subarachnoidal bleeding, but excluding transient ischemic attacks.

CNS, central nervous system; IC, intermediate care; ICU, intensive care unit.

Table 4

Pelvic Floor Distress Inventory Results

Variable	Time Frame	Surgical Treatment Comparison				BPMT Treatment Comparison			
		ULS N=188	SSLF N=186	Adjusted Mean Treatment Difference (95% CI)	*P* value	BPMT N=186	Usual Care N=188	Adjusted Mean Treatment Difference (95% CI)	*P* value
Urinary Distress Inventory (UDI) Score N Adjusted mean (SE) [Min, Max]	Baseline	175	179			178	176		
		123.0 (63.2)	130.0 (57.4)			128.1 (60.4)	124.9 (60.4)		
		[9.6, 292.3]	[28.2, 280.0]			[15.2, 280.0]	[9.6, 292.3]		
	Baseline to 6 Mo Change	163	165			163	165		
		−96.2 (5.9)	−99.7 (5.8)	3.6 (−9.6, 16.7)	0.60	−94.6 (4.9)	−87.9 (4.9)	−6.7 (−19.7, 6.2)	0.31
		[−276.5, 49.0]	[−256.0, 95.1]			[−276.5, 49.0]	[−264.0, 95.1]		
	Baseline to 12 Mo Change	153	159			156	156		
		−98.6 (5.9)	−98.3 (5.8)	−0.3 (−13.5, 12.9)	0.96	−91.7 (5.0)	−91.8 (4.9)	0.1 (−12.9, 13.2)	0.98
		[−276.5, 65.6]	[−244.0, 73.1]			[−276.5, 65.6]	[−259.2, 73.1]		
	Baseline to 24 Mo Change	144	148			146	146		
		−86.6 (5.9)	−88.4 (5.8)	1.8 (−11.5, 15.0)	0.79	−81.4 (5.0)	−80.1 (5.0)	−1.3 (−14.4, 11.8)	0.84
		[−274.6, 107.5]	[−261.5, 77.6]			[−274.6, 107.5]	[−242.4, 77.6]		
Pelvic Organ Prolapse Distress Inventory (POPDI) Score N Adjusted mean (SE) [Min, Max]	Baseline	175	179			178	176		
		120.2 (70.4)	127.4 (66.8)			126.0 (67.8)	121.6 (69.5)		
		[0.0, 300.0]	[0.0, 296.4]			[0.0, 300.0]	[7.1, 292.3]		
	Baseline to 6 Mo Change	163	165			163	165		
		−85.3 (6.2)	−91.7 (6.0)	6.5 (−7.5, 20.4)	0.36	−86.8 (5.3)	−73.2 (5.2)	−13.6 (−27.4, 0.2)	0.054
		[−267.3, 121.4]	[−278.0, 54.2]			[−267.3, 98.2]	[−278.0, 121.4]		
	Baseline to 12 Mo Change	153	159			156	156		
		−87.7 (6.2)	−93.0 (6.1)	5.3 (−8.8, 19.4)	0.46	−83.7 (5.3)	−80.0 (5.3)	−3.7 (−17.6, 10.3)	0.61
		[−241.7, 130.4]	[−273.2, 42.9]			[−263.7, 130.4]	[−273.2, 33.9]		
	Baseline to 24 Mo Change	144	148			146	146		
		−77.1 (6.2)	−78.6 (6.1)	1.5 (−12.7, 15.7)	0.84	−73.3 (5.4)	−65.2 (5.3)	−8.0 (−22.1, 6.1)	0.26
		[−252.4, 131.5]	[−288.7, 131.5]			[−252.4, 131.5]	[−288.7, 131.5]		

Variable	Time Frame	Surgical Treatment Comparison				BPMT Treatment Comparison			
		ULS N=188	SSLF N=186	Adjusted Mean Treatment Difference (95% CI)	*P* value	BPMT N=186	Usual Care N=188	Adjusted Mean Treatment Difference (95% CI)	*P* value
Colorectal-anal Distress Inventory (CRADI) Score N Adjusted mean (SE) [Min, Max]	Baseline	175	179			178	176		
		107.7 (85.6)	113.4 (82.2)			111.8 (85.5)	109.3 (82.3)		
		[0.0, 380.4]	[0.0, 357.1]			[0.0, 357.1]	[0.0, 380.4]		
	Baseline to 6 Mo Change	163	165			163	165		
		−67.7 (6.5)	−74.4 (6.4)	6.7 (−9.2, 22.7)	0.41	−67.9 (6.1)	−60.2 (6.0)	−7.7 (−23.6, 8.2)	0.34
		[−283.6, 84.5]	[−295.7, 89.5]			[−276.4, 64.3]	[−295.7, 89.5]		
	Baseline to 12 Mo Change	153	159			156	156		
		−73.0 (6.6)	−70.1 (6.4)	−2.9 (−19.0, 13.2)	0.73	−66.9 (6.1)	−61.7 (6.0)	−5.1 (−21.2, 10.9)	0.53
		[−363.3, 126.2]	[−295.7, 115.1]			[−269.3, 126.2]	[−363.3, 115.1]		
	Baseline to 24 Mo Change	144	148			146	146		
		−62.1 (6.6)	−51.1 (6.5)	−10.9 (−27.2, 5.3)	0.19	−52.5 (6.2)	−46.2 (6.1)	−6.3 (−22.5, 10.0)	0.45
		[−363.3, 96.7]	[−283.6, 206.2]			[−280.0, 151.5]	[−363.3, 206.2]		

CI=Confidence Interval; SE=Standard Error of Adjusted Mean.

NOTE: Patient reported outcome scale ranges: Pelvic Floor Distress Inventory (PFDI) scales, Urinary Distress Inventory (UDI) (0–300), Pelvic Organ Prolapse Distress Inventory (POPDI) (0–300), and Colorectal-anal Distress Inventory (CRADI) (0–400) with higher scores indicting greater symptom bother.