Published in final edited form as:

Int Urogynecol J. 2020 October ; 31(10): 2155–2164. doi:10.1007/s00192-020-04271-y.

Outcomes of Native Tissue Transvaginal Apical Approaches in Women with Advanced Pelvic Organ Prolapse and Stress Urinary Incontinence

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ClinicalTrials.gov Identifier: [NCT01166373](https://clinicaltrials.gov/ct2/show/study/NCT01166373)

The abstract was presented (oral presentation) at the Society of Gynecologic Surgeons 45th Annual Scientific Meeting in Tucson, Arizona, March 31 – April 3, 2019

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Abstract

Introduction and Hypothesis: Limited data exists comparing different surgical approaches in women with advanced vaginal prolapse. This study compared 2-year surgical outcomes of uterosacral ligament suspension (ULS) and sacrospinous ligament fixation (SSLF) in women with advanced prolapse (stage III–IV) and stress urinary incontinence.

Methods: This was a secondary analysis of a multicenter 2×2 factorial randomized trial comparing 1) ULS versus SSLF and 2) behavioral therapy with pelvic floor muscle training versus usual care. Of 374 subjects, 117/188 (62.7%) in ULS and 113/186 (60.7%) in SSLF had advanced prolapse. Two-year surgical success was defined by the absence of 1) apical descent >1/3 into vaginal canal, 2) anterior/posterior wall descent beyond the hymen, 3) bothersome bulge symptoms, and 4) retreatment for prolapse. Secondary outcomes included individual success outcome components, symptom severity measured by the Pelvic Organ Prolapse Distress Inventory, and adverse events. Outcomes were also compared in women with advanced prolapse versus stage II prolapse.

Results: Success did not differ between groups (ULS: 58.2% [57/117] versus SSLF: 58.5% [55/113], aOR 1.0 [0.5–1.8]). No differences were detected in individual success components ($p>0.05$ for all components). Prolapse symptom severity scores improved in both interventions with no intergroup differences ($p=0.82$). Serious adverse events did not differ (ULS: 19.7% versus SSLF: 16.8%, aOR 1.2 [0.6–2.4]). Success was lower in women with advanced prolapse compared to stage II (58.3% versus 73.2%, aOR 0.5 [0.3–0.9]), with no retreatment in stage II.

Conclusions: Surgical success, symptom severity, and overall serious adverse events did not differ between ULS and SSLF in women with advanced prolapse.

Brief summary:

In women with advanced vaginal prolapse and stress urinary incontinence, no difference was detected in 2-year surgical success and overall adverse events between uterosacral ligament suspension and sacrospinous ligament fixation.

Keywords

Advanced prolapse; pelvic organ prolapse; prolapse repair; sacrospinous ligament fixation; uterosacral ligament suspension; vaginal prolapse repair

Introduction

Approximately 300,000 pelvic organ prolapse surgeries are performed annually in the United States, most commonly via the transvaginal approach.[1–3] Lifetime surgical risk for pelvic organ prolapse is 13%, and up to 17% will undergo reoperation.[4, 5] Preoperative advanced prolapse stages have been shown to result in higher prolapse recurrence rates, likely a manifestation of more significant attenuation of pelvic floor support.[6–8] Despite the vaginal route being the most common surgical approach, there is a paucity of high-quality data regarding the impact of advanced preoperative prolapse stage on surgical outcomes comparing transvaginal prolapse surgeries; most published studies only address anatomic recurrence.[6–8]

The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD)-sponsored Pelvic Floor Disorder Network (PFDN) conducted a multicenter randomized controlled trial, the Operations and Pelvic Muscle Training in the Management of Apical Support Loss (OPTIMAL),[9] which provided the first direct comparative data of the two most common vaginal approaches, uterosacral ligament suspension (ULS) and sacrospinous ligament fixation (SSLF). The OPTIMAL trial demonstrated similar rates of surgical success at 2 years between the two approaches in a well-characterized cohort of women with preoperative prolapse stages II, III and IV analyzed as a combined group.[9]

Given the differences in biomechanical characteristics of the vaginal apex anchoring sites between ULS and SSLF, surgical outcomes could theoretically differ between the two approaches in women with advanced prolapse. The primary aim of this study was to compare 2-year surgical outcomes between USL and SSLF in women with advanced prolapse (stage III – IV) and stress urinary incontinence using data from the OPTIMAL trial. Secondly, surgical outcomes were compared between women with advanced versus (vs.) stage II prolapse.

Materials and Methods

Study Design

This was a secondary analysis of the previously published OPTIMAL trial.[9, 10] Institutional review board approval was obtained at each site, and participants provided written research informed consent. In the OPTIMAL trial, 374 women with pre-operative stages II through IV prolapse involving the apex were randomized in a 2×2 factorial design to one of the two native tissue transvaginal apical suspension procedures (ULS or SSLF), and behavioral intervention (perioperative behavioral therapy with pelvic floor muscle training [BPMT] or usual care). The surgical techniques (bilateral ULS and unilateral SSLF) have been described in the original study. [9, 10] All OPTIMAL participants had symptomatic stress urinary incontinence and underwent a concomitant mid-urethral sling.

Baseline demographics and clinical characteristics, anthropomorphic measurements, use of estrogen replacement therapy, previous hysterectomy, previous stress incontinence or pelvic organ prolapse surgery, and pelvic organ prolapse quantification system (POP-Q) were

obtained. Pelvic floor symptom severity was assessed using the subscales (Pelvic Organ Prolapse Distress Inventory [POPDI], Urinary Distress Inventory [UDI], and Colorectal-Anal Distress Inventory [CRADI]) of the Pelvic Floor Distress Inventory (PFDI, range 0 [least impact] to 300 [most impact]).[11, 12]

Outcomes

This secondary analysis was designed to primarily compare surgical outcomes of ULS vs. SSLF in a subset of women with preoperative advanced prolapse (stage III – IV) from the OPTIMAL cohort. The primary outcome of surgical success, assessed at 2 years, used a composite outcome measure. “Success” was defined by the absence of all of the following; 1) vaginal apical descent 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 PFDI[11] and any response other than “not at all” to the question “How much does this bother you?”, and 4) retreatment for prolapse (surgery or pessary).

Because no consensus exists to define success for prolapse surgeries, in addition to the primary success definition, which is identical to the original OPTIMAL primary outcome,[9] two alternative composite success definitions with less strict vaginal apex criteria commonly used in other existing studies were explored.[13] Specifically, the vaginal apex component of the composite success definition was replaced with the absence of i) descent of the vaginal apex more than one-half into the vaginal canal (“Success Definition #2”), or ii) descent of the vaginal apex beyond the hymen (“Success Definition #3”). Secondary outcomes, also measured at 2 years, include individual success components, pelvic floor symptom severity assessed by the changes in PFDI[11] subscale scores, and adverse events (classified as serious/non-serious and expected/unexpected as described in the original study).[9, 10] Exploratory analyses were also conducted to compare the primary and secondary outcomes as described above in women with advanced vs. stage II prolapse.

Statistical Analysis

Bivariate analyses of baseline demographic and clinical characteristics were performed using Student’s t-, Mann-Whitney U, chi-square, or Fisher’s exact tests as appropriate. Outcomes were evaluated via generalized linear mixed models with a logit link if binary, and general linear mixed models if continuous. Adjusted models included terms for prolapse severity, surgical group assignment, BPMT assignment, and their interactions, concomitant hysterectomy, and a random effect for surgeon. For outcomes that were too infrequent to permit modeling, comparisons were conducted using Fisher’s exact tests. Surgical success and other outcomes were compared between surgical assignments, prolapse severity categories, and combinations of the two. A p value of less than 0.05 was considered statistically significant. All statistical analyses were conducted using SAS Version 9.4 (SAS Institute Inc., Cary, NC).

Results:

Surgical Outcomes of USL vs. SSLF in Women with Advanced Prolapse

Of 374 subjects, 117/188 (62.7%) in ULS and 113/186 (60.7%) in the SSLF group had advanced prolapse. No intergroup difference was noted in missing data for any of the outcomes for this secondary analysis (data not shown). Table 1 displays baseline demographics and clinical characteristics of women with advanced prolapse, which were similar between surgical groups except for the median number of vaginal deliveries.

Composite surgical success at 2 years, using the original OPTIMAL success definition,[9] did not differ between groups (ULS 58.2% vs. SSLF 58.5%, adjusted odds ratio [aOR] 1.0, 95% confidence interval [CI]: 0.5, 1.8, Table 2). Replacing with less strict anatomic criteria for the apex in the composite success definition (changing from “no apical descent >1/3 into vaginal canal” to “no apical descent > 1/2 into vaginal canal” [Success Definition #2], and “no apical descent beyond the hymen” [Success Definition #3]), small increases were noted in success rates for both definitions without detectable differences between ULS and SSLF groups (Table 2).

Further, the analyses of individual anatomic success components by compartment (anterior, posterior, apical) demonstrated no differences between surgical groups. Overall anatomic failure (the leading edge of prolapse beyond the hymen) rates of 20% or less occurred primarily in the anterior compartment and only 1% at the apex (Table 2). Bothersome vaginal bulge symptoms were also similar between groups (ULS 18.9% vs. SSLF 21.1%, aOR 0.9, 95% CI 0.4, 1.8) at 2 years, and retreatment was equally uncommon in both groups (ULS 8.0% vs. SSLF 8.3%, $p=1.00$, Table 2).

Prolapse symptom severity measured by POPDI scores improved from baseline at 2 years in both groups, with no intergroup difference noted (ULS unadjusted mean $\pm$ standard deviation -72.7 ± 67.4 vs. SSLF -74.1 ± 72.2 , adjusted mean difference 2.4, 95% CI: -17.9 , 22.6 , Table 2). Urinary and bowel symptom severity measured by UDI and CRADI, respectively, was also not different between groups (Table 2).

Among women with advanced prolapse, no difference in serious adverse events was detected between groups (ULS 19.7% vs. SSLF 16.8%, aOR 1.2, 95% CI: 0.6, 2.4, Table 3). Similar rates were noted for intraoperative complications (bladder injury, ureteral obstruction) and postoperative adverse events up to 2 years (Table 3).

Surgical Outcomes in Women with Advanced vs. Stage II Prolapse

In the OPTIMAL trial, 230 (61.5%) women had advanced prolapse, and 144 (38.5%) had stage II prolapse. These groups differed in age, median number of vaginal deliveries, menopausal status, current use of vaginal estrogen, and preoperative POP-Q values between groups (Table 1). Success at 2 years was lower in those with advanced prolapse compared to stage II (58.3% vs. 73.2%, aOR 0.5, 95% CI: 0.3, 0.9, Table 2). Further, composite success in women with advanced vs. stage II prolapse was explored by surgical approach; however, no difference in success rate of advanced vs. stage II was detected between the ULS and

SSLF groups (no significant interaction between surgical procedure and prolapse severity, $p=0.19$).

Using alternative composite success definitions with less strict anatomic criteria, surgical success remained lower in women with advanced prolapse (Success Definition #2 and #3, Table 2). Furthermore, women with advanced prolapse had a higher rate of prolapse beyond the hymen (18.9% vs. 7.7%, aOR 2.8, 95% CI: 1.1, 6.8), predominantly in the anterior compartment (aOR 3.9, 95% CI: 1.4, 10.7, Table 2). While no difference was noted in bothersome vaginal bulge symptoms comparing advanced vs. stage II prolapse (advanced: 20.0% vs. stage II: 15.0%, aOR 1.5, 95% CI: 0.8, 2.9), retreatment for prolapse (either surgery or pessary) was higher in women with advanced prolapse (8.2% vs. 0%, $p<0.01$, Table 2).

Prolapse symptom severity measured by POPDI scores improved in both advanced prolapse and stage II groups at 2 years, with no detected difference based on initial prolapse severity (Table 2). Urinary and bowel symptom severity also improved at 2 years in both groups. A greater reduction in CRADI scores was observed in the stage II prolapse group compared to advanced prolapse (Table 2). No difference was noted in adverse events in women with advanced vs. stage II prolapse (Table 3).

Discussion

In women with advanced vaginal prolapse and stress urinary incontinence undergoing transvaginal native tissue prolapse procedures with a midurethral sling, the current study did not detect a difference in overall surgical success at 2 years between women undergoing ULS vs. SSLF (ULS 58.2% vs. SSLF 58.5%, aOR 1.0, 95% CI: 0.5, 1.8). This is consistent with the primary success rate reported in the index OPTIMAL trial which included women with stage II to IV prolapse (ULS 64.5% vs. SSLF 63.1%, aOR 1.1, 95% CI: 0.7, 1.7).[9] Surgical success was defined by composite criteria using strict anatomic criteria of neither apical descent greater than 1/3 into the vaginal canal nor anterior/posterior vaginal wall beyond hymen in addition to the absence of bothersome vaginal bulge symptoms or retreatment at 2 years.

No consensus exists regarding the definition of “success” for prolapse surgeries. As a consequence, there is a wide range of reported treatment success rates in the current literature.[13] This study explored alternative composite success definitions using less strict apical descent criteria, resulting in slightly increased success rates in both surgery groups without detecting intergroup differences. Prolapse recurrence by individual anatomic compartment in women with advanced prolapse revealed that the majority of recurrences occurred in the anterior compartment with no difference detected between surgical interventions, consistent with other studies including the index OPTIMAL trial.[9, 14, 15]

The relatively low success rate (58%) in women with advanced prolapse in the current study is possibly due to the stringent composite success definition (both anatomic and subjective criteria) used in the study (as was in the original OPTIMAL study). Patient reported outcome measures have been recognized as a critical component in defining success for

pelvic floor surgical outcome studies, as anatomical findings do not often correlate with patient experience and their perception of symptom improvement. Using the relatively strict anatomic criteria, especially in women with advanced stage prolapse, it is possible that some women met the “failure” criteria solely based on their anatomy, even if they noticed great improvement postoperatively compared to their baseline anatomy. In addition, the subjective failure definition was also very stringent, which was defined as having any answer other than “not at all” for having a bothersome vaginal bulge. This is evident from the significant improvement in POPDI scores noted in both groups (-72.7 vs. -74.1 , with no difference between ULS vs. SSLF), which is a validated measure to assess prolapse symptom severity. This could explain the low retreatment rates demonstrated in the current study (8% in advanced prolapse group, and none in stage II).

Previous studies examined the risk of surgical failure in women with advanced preoperative prolapse stages; however, the majority of data are based on anatomic criteria only.[6–8] One study reported that women with baseline POP-Q stage III – IV had a higher rate of anatomical recurrence after vaginal prolapse repair compared to women with stage II (OR 2.7, 95% CI: 1.3, 5.3).[7] A meta-analysis of outcomes of transvaginal ULS demonstrated no differences in the rate of postoperative anterior compartment recurrence in women with preoperative stage III prolapse compared to stage II (33% versus 8%, $p=0.06$).[6] In the current study, in addition to having greater odds of anatomic failure in women with advanced prolapse, composite success was significantly lower in advanced prolapse (aOR 0.5, 95% CI: 0.3, 0.9), and only women with preoperative advanced stage prolapse underwent retreatment (surgery or pessary) by 2 years.

In women with advanced prolapse, adverse events were relatively rare; differences in adverse events (overall serious events as well as individual events) were not statistically significant between the surgical groups. Similarly, no difference in adverse events was detected comparing women with advanced vs. stage II prolapse.

Limitations of this study include that these results are applicable only to women undergoing transvaginal prolapse repair with a concomitant mid-urethral sling for stress urinary incontinence. In the index OPTIMAL trial with the 2×2 factorial design, participants were also randomized to behavioral intervention. However, all of the outcomes reported in this study were adjusted for BPMT assignment and its interactions with prolapse severity and surgical intervention assignment. Additionally, given the inherent nature of secondary analysis, this study may not be sufficiently powered to detect a significant difference for our primary outcome between surgical groups within a subset of the original OPTIMAL participants. However, the observed difference between SSLF and ULS (0.3%) in this analysis of women with advanced prolapse is not clinically meaningful, and designing a study to find such a small difference would not be feasible.

Strengths include generalizability as the study population included a well characterized cohort of a large number of participants recruited from 10 sites across the US. Additionally, the surgical interventions were randomized to minimize potential bias. Furthermore, to account for the lack of consensus on anatomic surgical “success”, various definitions of

success were explored, in addition to addressing individual success components commonly reported in the literature.

The current study provides useful information for patient counseling and decision making, specifically with respect to the effectiveness and safety of the two most commonly performed native tissue vaginal surgeries for apical prolapse. Due to limited evidence, surgeons often face a challenge when considering a surgical approach, and the decision is typically made based on their experience with regard to preventing recurrence in women with advanced prolapse. This study did not detect any difference in treatment success, assessed by various success criteria, between ULS and SSLF at 2 years postoperatively in women with advanced prolapse and stress urinary incontinence; however, success was lower compared to women with stage II prolapse. No women with stage II prolapse at baseline underwent retreatment for prolapse by 2 years. Continued efforts are warranted to examine durability between the transvaginal native tissue prolapse repair techniques in women with advanced prolapse as well as to expand to other surgical approaches via different surgical routes including those with and without graft use for apical prolapse.

Acknowledgements

In addition to the authors, the following members of the Pelvic Floor Disorders Network participated in the Operations and Pelvic Muscle Training in the Management of Apical Support Loss (OPTIMAL) trial:

RTI International: Klein Warren, Lauren, Matthews, Daryl, Shaffer, Amanda, Terry, Tamara T, Thornberry, Jutta, Wallace, Dennis, Wilson, Kevin A, Hartmann, Katherine

University of Alabama at Birmingham: Ballard, Alicia, Burge, Julie, Burgio, Kathryn L, Carter, Kathy, Goode, Patricia S, Markland, Alayne D, Pair, Lisa S, Parker-Autry, Candace, Varner, R Edward, Wilson, Tracey S

Duke University: Amundsen, Cindy L, Harm-Ernandes, Ingrid, Raynor, Mary, Siddiqui, Nazema Y, Weidner, Alison C, Wu, Jennifer M

University of California at San Diego: Albo, Michael E, Grimes, Cara

Nager, Charles W

Kaiser Permanente - Downey: Nguyen, John N

Kaiser Permanente - Bellflower: Jakus-Waldman, S

Kaiser Permanente – San Diego: Diwadkar, Gouri, Dyer, Keisha Y, Hall, Lynn M, Mackinnon, Linda M, Menefee, Shawn A, Tan-Kim, Jasmine, Zazueta-Damian, Gisselle

University of Texas-Southwestern: Atnip, Shanna, Moore, Elva Kelly, Rahn, David, Schaffer, Joseph

University of Pittsburgh: Borello-France, D

Former NICHD: Meikle, Susan F

Cleveland Clinic: Barber, Matthew D, Frick, Anna, Jelovsek, John Eric, O'Dougherty, Betsy, Paraiso, Marie FR, Pung, Ly, Ridgeway, Beri M, Williams, Cheryl

Loyola University Chicago: Brubaker, Linda, Mueller, Elizabeth, Tulke, Mary

University of Michigan: Casher, Yang Wang, Chen, Yeh-Hsin, DiFranco, Donna, Marchant, Bev, Spino, Cathie, Wei, John T

University of Utah Medical Center: Baker, Jan, Hsu, Yvonne, Masters, Maria, Orr, Amy

Author Disclosures:

I Meyer/RE Whitworth/AL Smith/VW Sung/MF Ackenbom/C Wai: No conflict of interest ES Lukacz: Research Support: Boston Scientific, Uroplasty/Cogentix, Pfizer; Consultant: Axonics

AG Visco: Stock ownership: NinoMed

D Mazloomdoost: Research Grant: Boston Scientific

MG Gantz: Research Grant: Boston Scientific

HE Richter: Research Grant: Renovia, Allergan;

Financial Support:

Supported by grants from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (UG1 HD054241, UG1 HD041261, UG1 HD054214, UG1 HD041267, UG1 HD069010, UG1 HD069006, UG1 HD069013, U24 HD069031) and the National Institutes of Health Office of Research on Women's Health.

References:

1. FDA, Urogynecologic surgical mesh: update on the safety and effectiveness of transvaginal mesh placement for pelvic organ prolapse. US Food and Drug Administration, 2011: p. US Food and Drug Administration; 2011.
2. Boyles SH, Weber AM, and Meyn L, Procedures for pelvic organ prolapse in the United States, 1979–1997. *Am J Obstet Gynecol*, 2003 188(1): p. 108–15. [PubMed: 12548203]
3. Montoya TI, Grande KB, and Rahn DD, Apical vaginal prolapse surgery: practice patterns and factors guiding route of repair. *Female Pelvic Med Reconstr Surg*, 2012 18(6): p. 315–20. [PubMed: 23143421]
4. Wu JM, et al., Prevalence and trends of symptomatic pelvic floor disorders in U.S. women. *Obstet Gynecol*, 2014 123(1): p. 141–8. [PubMed: 24463674]
5. Denman MA, et al., Reoperation 10 years after surgically managed pelvic organ prolapse and urinary incontinence. *Am J Obstet Gynecol*, 2008 198(5): p. 555 e1–5. [PubMed: 18355779]
6. Margulies RU, Rogers MA, and Morgan DM, Outcomes of transvaginal uterosacral ligament suspension: systematic review and metaanalysis. *Am J Obstet Gynecol*, 2010 202(2): p. 124–34. [PubMed: 20113690]
7. Whiteside JL, et al., Risk factors for prolapse recurrence after vaginal repair. *Am J Obstet Gynecol*, 2004 191(5): p. 1533–8. [PubMed: 15547521]
8. Qatawneh A, et al., Risk factors of surgical failure following sacrospinous colpopexy for the treatment of uterovaginal prolapse. *Arch Gynecol Obstet*, 2013 287(6): p. 1159–65. [PubMed: 23269355]
9. Barber MD, et al., Comparison of 2 transvaginal surgical approaches and perioperative behavioral therapy for apical vaginal prolapse: the OPTIMAL randomized trial. *JAMA*, 2014 311(10): p. 1023–34. [PubMed: 24618964]
10. Barber MD, et al., Operations and pelvic muscle training in the management of apical support loss (OPTIMAL) trial: design and methods. *Contemp Clin Trials*, 2009 30(2): p. 178–89. [PubMed: 19130903]
11. Barber MD, et al., Psychometric evaluation of 2 comprehensive condition-specific quality of life instruments for women with pelvic floor disorders. *Am J Obstet Gynecol*, 2001 185(6): p. 1388–95. [PubMed: 11744914]
12. Barber MD, Walters MD, and Bump RC, Short forms of two condition-specific quality-of-life questionnaires for women with pelvic floor disorders (PFDI-20 and PFIQ-7). *Am J Obstet Gynecol*, 2005 193(1): p. 103–13. [PubMed: 16021067]
13. Barber MD, et al., Defining success after surgery for pelvic organ prolapse. *Obstet Gynecol*, 2009 114(3): p. 600–9. [PubMed: 19701041]

14. Fialkow MF, Newton KM, and Weiss NS, Incidence of recurrent pelvic organ prolapse 10 years following primary surgical management: a retrospective cohort study. *Int Urogynecol J Pelvic Floor Dysfunct*, 2008 19(11): p. 1483–7. [PubMed: 18682876]
15. Morgan DM, et al., Heterogeneity in anatomic outcome of sacrospinous ligament fixation for prolapse: a systematic review. *Obstet Gynecol*, 2007 109(6): p. 1424–33. [PubMed: 17540817]

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Table 1:

Baseline Demographics and Characteristics

Characteristic	Category	Apical Suspension Procedure				Comparison Advanced Prolapse				Advanced vs. Stage II Prolapse		
		ULS (N=117)	SSLF (N=113)	ULS vs. SSLF Difference (95% CI)	P	Advanced (N=230)	Stage II (N=144)	Advanced vs. Stage II Difference (95% CI)	P			
Age, mean (SD), years		60.7 (10.4)	60.6 (10.3)	0.1 (−2.6, 2.8)	0.94	60.7 (10.3)	51.7 (9.3)	−9.0 (−11.1, −6.9)	<0.01			
Race	White	98 (83.8%)	95 (84.1%)	−0.3% (−13.3%, 12.5%)	0.19	193 (83.9%)	122 (84.7%)	0.8% (−9.6%, 11.2%)	0.94			
	Black	6 (5.1%)	9 (8.0%)	−2.8% (−15.9%, 10%)		15 (6.5%)	7 (4.9%)	−1.7% (−12.1%, 8.7%)				
	Asian	0 (0.0%)	2 (1.8%)	−1.8% (−14.8%, 11.3%)		2 (0.9%)	2 (1.4%)	0.5% (−9.9%, 10.9%)				
	American Indian/ Alaska Native	0 (0.0%)	1 (0.9%)	−0.9% (−13.9%, 12.1%)		1 (0.4%)	1 (0.7%)	0.3% (−10.1%, 10.7%)				
	Other	13 (11.1%)	6 (5.3%)	5.8% (−7.3%, 18.5%)		19 (8.3%)	12 (8.3%)	0.1% (−10.3%, 10.4%)				
Hispanic ethnicity		27 (23.1%)	19 (16.8%)	6.3% (−6.7%, 19.2%)	0.24	46 (20.0%)	29 (20.1%)	0.1% (−10.3%, 10.5%)	0.97			
Insurance: Private/HMO		79 (67.5%)	74 (65.5%)	2% (−10.8%, 15%)	0.74	153 (66.5%)	98 (68.1%)	1.5% (−8.9%, 11.9%)	0.76			
Insurance: Medicaid/ Medicare		47 (40.2%)	42 (37.2%)	3% (−10%, 15.9%)	0.64	89 (38.7%)	20 (13.9%)	−24.8% (−34.7%, −14.5%)	<0.01			
Insurance: Self-pay		0 (0.0%)	1 (0.9%)	−0.9% (−13.9%, 12.1%)	0.31	1 (0.4%)	5 (3.5%)	3% (−7.4%, 13.4%)	0.02			
Insurance: Other		22 (18.8%)	18 (15.9%)	2.9% (−10%, 15.9%)	0.57	40 (17.4%)	32 (22.2%)	4.8% (−5.6%, 15.2%)	0.25			
Vaginal deliveries, median (IQR)		3.0 (2.0, 5.0)	3.0 (2.0, 4.0)	0.6 (0.1, 1.1)	0.03	3.0 (2.0, 4.0)	2.0 (2.0, 3.0)	−0.6 (−1.0, −0.3)	<0.01			
Cesarean deliveries, median (IQR)		0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (−0.1, 0.1)	0.84	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	−0.0 (−0.1, 0.1)	0.35			
Menstrual status	Premenopausal	25 (21.4%)	20 (17.7%)	3.7% (−9.3%, 16.7%)	0.61	45 (19.6%)	61 (42.4%)	22.8% (12.5%, 32.8%)	<0.01			
	Postmenopausal	89 (76.1%)	88 (77.9%)	−1.8% (−14.8%, 11.2%)		177 (77.0%)	69 (47.9%)	−29% (−38.8%, −18.9%)				
	Not sure	3 (2.6%)	5 (4.4%)	−1.9% (−14.9%, 11.1%)		8 (3.5%)	14 (9.7%)	6.2% (−4.2%, 16.5%)				
Currently using estrogen therapy: Oral/patch		10 (8.5%)	20 (17.7%)	−9.2% (−21.9%, 3.9%)	0.05	30 (13.0%)	16 (11.1%)	−1.9% (−12.3%, 8.4%)	0.58			
Currently using estrogen therapy: Vaginal		25 (21.4%)	18 (15.9%)	5.4% (−7.5%, 18.4%)	0.29	43 (18.7%)	45 (31.3%)	12.6% (2.1%, 22.8%)	<0.01			
Current smoker		5 (4.3%)	10 (8.8%)	−4.6% (−17.6%, 8.3%)	0.16	15 (6.5%)	18 (12.5%)	6% (−4.5%, 16.3%)	0.05			

		Apical Suspension Procedure Comparison Advanced Prolapse					Advanced vs. Stage II Prolapse			
Characteristic	Category	ULS (N=117)	SSLF (N=113)	ULS vs. SSLF Difference (95% CI)	P	Advanced (N=230)	Stage II (N=144)	Advanced vs. Stage II Difference (95% CI)	P	
Diabetes mellitus		14 (12.1%)	15 (13.6%)	-1.6% (-14.5%, 11.6%)	0.72	29 (12.8%)	15 (10.7%)	-2.1% (-12.6%, 8.4%)	0.54	
Connective tissue disease (SLE, Marfans, Sjogren, Scleroderma)		3 (2.6%)	1 (0.9%)	1.7% (-11.5%, 14.9%)	0.32	4 (1.8%)	1 (0.7%)	-1.1% (-11.5%, 9.4%)	0.39	
Prior hysterectomy		31 (26.5%)	36 (31.9%)	-5.4% (-18.3%, 7.6%)	0.37	67 (29.1%)	33 (22.9%)	-6.2% (-16.5%, 4.2%)	0.19	
Prior stress urinary incontinence surgery		3 (2.6%)	3 (2.7%)	-0.1% (-13.1%, 12.9%)	0.97	6 (2.6%)	7 (4.9%)	2.3% (-8.2%, 12.6%)	0.25	
Prior pelvic organ prolapse surgery		5 (4.3%)	11 (9.7%)	-5.5% (-18.4%, 7.4%)	0.10	16 (7.0%)	10 (6.9%)	0% (-10.4%, 10.3%)	>0.99	
BMI, mean (SD) kg/m ²		28.8 (5.0)	28.7 (5.8)	0.2 (-1.2, 1.6)	0.80	28.8 (5.4)	29.0 (5.6)	0.2 (-0.9, 1.4)	0.69	
Randomized BPMT Arm	PMT	56 (47.9%)	58 (51.3%)	-3.5% (-16.5%, 9.6%)	0.60	114 (49.6%)	72 (50.0%)	0.4% (-10%, 10.8%)	0.93	
	USUAL CARE	61 (52.1%)	55 (48.7%)	3.5% (-9.6%, 16.5%)		116 (50.4%)	72 (50.0%)	-0.4% (-10.8%, 10%)		
POP-Q stage	Stage III	110 (94.0%)	102 (90.3%)	3.8% (-9.1%, 16.7%)	0.29	212 (92.2%)	0 (0.0%)	-92.2% (-95.7%, -86.7%)	<0.01	
	Stage IV	7 (6.0%)	11 (9.7%)	-3.8% (-16.7%, 9.1%)		18 (7.8%)	0 (0.0%)	-7.8% (-18.2%, 2.6%)		
Maximum descent of any segment, mean (SD)		3.3 (1.7)	3.7 (1.9)	-0.4 (-0.8, 0.1)	0.12	3.5 (1.8)	0.4 (0.7)	-3.1 (-3.4, -2.8)		
POP-Q value: Ba, median (IQR) cm		3.0 (2.0, 4.0)	3.0 (2.0, 4.0)	-0.2 (-0.7, 0.3)	0.47	3.0 (2.0, 4.0)	0.0 (0.0, 1.0)	-3.0 (-3.3, -2.6)	<0.01	
POP-Q value: C, median (IQR) cm		0.0 (-3.0, 2.0)	1.0 (-3.0, 3.0)	-0.9 (-1.9, -0.0)	0.05	0.0 (-3.0, 3.0)	-3.0 (-4.0, -2.0)	-3.3 (-4.0, -2.7)	<0.01	
POP-Q value: Bp, median (IQR) cm		-1.0 (-2.0, 0.0)	-1.0 (-2.0, 1.0)	-0.7 (-1.3, -0.0)	0.05	-1.0 (-2.0, 0.5)	-2.0 (-2.0, 0.0)	-1.0 (-1.5, -0.5)	<0.01	
POP-Q value: GH, median (IQR) cm		5.0 (4.0, 6.0)	5.0 (4.0, 6.0)	-0.1 (-0.4, 0.3)	0.78	5.0 (4.0, 6.0)	4.0 (4.0, 5.0)	-0.6 (-0.9, -0.3)	<0.01	
POP-Q value: PB, median (IQR) cm		3.0 (3.0, 4.0)	3.0 (3.0, 4.0)	0.0 (-0.2, 0.3)	0.77	3.0 (3.0, 4.0)	3.5 (3.0, 4.0)	0.2 (0.0, 0.4)	<0.01	
POP-Q value: TVL, median (IQR) cm		9.0 (8.0, 10.0)	9.0 (8.0, 10.0)	0.0 (-0.3, 0.3)	0.94	9.0 (8.0, 10.0)	10.0 (9.0, 10.0)	0.5 (0.3, 0.8)	0.03	
Baseline Quality of Life	POPDI	120.2 (70.4)	127.4 (66.8)	-4.9 (-23.1, 13.3)	0.60	121.8 (67.4)	127.1 (70.5)	7.0 (-7.8, 21.8)	0.35	
Assessment Score, mean (SD)	UDI	123.0 (63.2)	130.0 (57.4)	-7.7 (-23.7, 8.3)	0.34	121.9 (58.5)	134.0 (62.6)	13.5 (0.5, 26.5)	0.04	
	CRADI	107.7 (85.6)	113.4 (82.2)	5.7 (-16.3, 27.7)	0.61	101.6 (79.8)	125.1 (88.3)	24.5 (6.6, 42.4)	0.01	

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SD = Standard deviation
HMO = Health Maintenance organization
IQR = Inter-quartile Range
SLE = Systemic Lupus Erythematosis
BMI = Body Mass Index
BPMT = Behavioral therapy with Pelvic floor Muscle Training
POP-Q = Pelvic Organ Prolapse Quantification
GH = Genital Hiatus
PB = Perineal Body
TVL = Total Vaginal Length

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Table 2:

Pelvic Organ Prolapse & Pelvic Floor Symptom Severity Outcomes at 2 years

Characteristic	Apical Suspension Procedure				Comparison Advanced Prolapse				Advanced vs. Stage II Prolapse			
	ULS (N=117)	SSLF (N=113)	Adjusted OR 95%CI	P	Advanced (N=230)	Stage II (N=144)	Adjusted OR (95% CI)	P				
<u>Composite Surgical Success:</u>												
Definition #1 [APICAL DESCENT (C -2/3 TVL)]	57 (58.2%)	55 (58.5%)	1.0 (0.5, 1.8)	0.94	112 (58.3%)	82 (73.2%)	0.5 (0.3, 0.9)	0.02				
Definition #2 [APICAL DESCENT (C -1/2 TVL)]	59 (60.8%)	62 (66.7%)	0.8 (0.4, 1.4)	0.42	121 (63.7%)	84 (75.7%)	0.6 (0.3, 1.0)	0.05				
Definition #3 [APICAL PROLAPSE (C 0)]	59 (60.8%)	62 (66.7%)	0.8 (0.4, 1.4)	0.42	121 (63.7%)	84 (75.7%)	0.6 (0.3, 1.0)	0.05				
<u>Anatomic Failure:</u>												
Prolapse beyond the hymen: Leading edge > 0	19 (20.0%)	17 (17.9%)	1.2 (0.5, 2.5)	0.70	36 (18.9%)	9 (7.7%)	2.8 (1.1, 6.8)	0.02				
Prolapse beyond the hymen: Anterior (POPQ Ba >0)	17 (17.9%)	16 (16.8%)	1.1 (0.5, 2.4)	0.77	33 (17.4%)	7 (5.9%)	3.9 (1.4, 10.7)	0.01				
Prolapse beyond the hymen: Posterior (POPQ Bp >0)	2 (2.1%)	2 (2.1%)	NA - LN ^{#1}	1.00	4 (2.1%)	4 (3.4%)	NA - LN ^{#1}	0.49				
Prolapse beyond the hymen: Apical (POPQ C>0)	1 (1.1%)	1 (1.1%)	NA - LN ^{#1}	1.00	2 (1.1%)	2 (1.7%)	NA - LN ^{#1}	0.64				
Apical descent >1/3 of TVL (C> -2/3 TVL) [‡]	12 (12.6%)	16 (16.8%)	0.7 (0.3, 1.6)	0.39	28 (14.7%)	9 (7.7%)	NA - LN ^{#1}	0.07				
Apical descent >1/2 of TVL (C> -1/2 TVL)	2 (2.1%)	4 (4.2%)	NA - LN ^{#1}	0.69	6 (3.2%)	2 (1.7%)	NA - LN ^{#1}	0.71				
Symptom Failure: Botherome Bulse Symptoms [‡]	17 (18.9%)	20 (21.1%)	0.9 (0.4, 1.8)	0.69	37 (20.0%)	18 (15.0%)	1.5 (0.8, 2.9)	0.21				
Retreatment for POP: Either Surevry or Pessary	8 (8.0%)	8 (8.3%)	NA ^{#2}	1.00	16 (8.2%)	0 (0.0%)	NA ^{#2}	<0.01				
Retreatment for POP: Surgery	5 (5.0%)	4 (4.2%)	NA ^{#2}	1.00	9 (4.6%)	0 (0.0%)	NA ^{#2}	0.01				
Retreatment for POP: Pessary [‡]	5 (5.0%)	5 (5.2%)	NA ^{#2}	1.00	10 (5.1%)	0 (0.0%)	NA ^{#2}	0.02				
<u>Symptom Severity Scores:</u> Change from Baseline to 2 years												
POPDI	-72.7 (67.4)	-74.1 (72.2)	2.4 (-17.9, 22.6) ^{#3}	0.82	-70.8 (72.8)	-77.6 (64.8)	-7.1 (-23.4, 9.2) ^{#3}	0.39				
UDI	-82.7 (63.1)	-86.5 (66.4)	3.9 (-20.2, 28.0) ^{#3}	0.75	-79.2 (63.4)	-93.3 (66.1)	-15.1 (-36.9, 6.6) ^{#3}	0.17				
CRADI	-56.8 (74.4)	-47.5 (86.1)	-18.6 (-42.1, 5.0) ^{#3}	0.12	-44.6 (80.9)	-63.9 (78.9)	-19.7 (-38.6, -0.7) ^{#3}	0.04				

Composite Surgical success definitions also include absence of: anterior or posterior vaginal wall descent beyond the hymen (any of the POPQ points, Ba, Bp are > 0cm), bothersome vaginal bulge symptoms using the PFDI questions, and retreatment for prolapse.

Unless otherwise noted below, models adjust for concomitant hysterectomy, surgeon, BPMT treatment assignment, surgical assignment, baseline POPQ severity and all interactions between variables with an asterisk.

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[†] Surgeon was removed from the model to achieve convergence.

[‡]

[§] Result(s) not shown because of low numbers leading to low reliability of test. Unadjusted Fisher's exact test p-value reported.

^{*2} Unadjusted Fisher's exact test results shown because there are zero outcomes in one group; also done for retreatment outcomes because all occurred in the severe prolapse group and were distributed evenly between the surgical groups.

^{*3} Adjusted mean difference (95% CI)

Table 3:

Adverse Events

Characteristic	Apical Suspension Procedure Comparison Advanced Prolapse				Advanced vs. Stage II Prolapse			
	ULS (N=117)	SSLF (N=113)	Adjusted OR (95% CI)	P	Advanced (N=230)	Stage II (N=144)	Adjusted OR (95% CI)	P
Participants with any Adverse Event (AE) [†]	88 (75.2%)	85 (75.2%)	1.0 (0.5, 1.8)	0.95	173 (75.2%)	109 (75.7%)	1.0 (0.6, 1.6)	0.94
Serious AE [‡]	23 (19.7%)	19 (16.8%)	1.2 (0.6, 2.4)	0.61	42 (18.3%)	20 (13.9%)	1.4 (0.8, 2.6)	0.26
Expected AE [‡]	79 (67.5%)	79 (69.9%)	0.9 (0.5, 1.5)	0.64	158 (68.7%)	102 (70.8%)	0.9 (0.6, 1.5)	0.71
Bladder injury	13 (11.1%)	7 (6.2%)	1.7 (0.6, 5.2)	0.33	20 (8.7%)	20 (13.9%)	0.7 (0.3, 1.8)	0.47
Bladder injury: During mid-urethral sling [‡]	11 (9.4%)	7 (6.2%)	1.5 (0.5, 4.6)	0.45	18 (7.8%)	18 (12.5%)	NA - LN ^{*I}	0.15
Bladder injury: Other	2 (1.7%)	0 (0.0%)	NA ^{*2}	0.50	2 (0.9%)	2 (1.4%)	NA - LN ^{*I}	0.64
Ureteral obstruction (Intraoperative & Delayed recognition)	5 (4.3%)	0 (0.0%)	NA ^{*2}	0.06	5 (2.2%)	1 (0.7%)	NA - LN ^{*I}	0.41
Intraoperative ureteral obstruction: Treatment=Suture removed intraop	4 (3.4%)	0 (0.0%)	NA ^{*2}	0.12	4 (1.7%)	1 (0.7%)	NA - LN ^{*I}	0.65
Intraoperative ureteral obstruction: Treatment=Stent placed intraop	1 (0.9%)	0 (0.0%)	NA ^{*2}	1.00	1 (0.4%)	0 (0.0%)	NA ^{*2}	1.00
Ureteral injury - Delayed recognition	1 (0.9%)	0 (0.0%)	NA ^{*2}	1.00	1 (0.4%)	0 (0.0%)	NA ^{*2}	1.00
Blood transfusion [‡]	6 (5.1%)	4 (3.5%)	1.5 (0.4, 6.5)	0.57	10 (4.3%)	1 (0.7%)	NA - LN ^{*I}	0.06
Neurologic pain requiring treatment ^a	7 (6.0%)	11 (9.7%)	0.5 (0.2, 1.4)	0.18	18 (7.8%)	18 (12.5%)	0.6 (0.3, 1.2)	0.13
Neurologic pain requiring treatment: Narcotic pain medication ^a	7 (6.0%)	8 (7.1%)	0.7 (0.2, 2.1)	0.51	15 (6.5%)	13 (9.0%)	NA - LN ^{*I}	0.42
Neurologic pain requiring treatment: Nerve block ^a	0 (0.0%)	1 (0.9%)	NA ^{*2}	0.49	1 (0.4%)	1 (0.7%)	NA - LN ^{*I}	1.00
Neurologic pain requiring treatment: Physical therapy ^a	1 (0.9%)	2 (1.8%)	NA - LN ^{*I}	0.62	3 (1.3%)	2 (1.4%)	NA - LN ^{*I}	1.00
Neurologic pain requiring treatment: Other medication ^a	2 (1.7%)	7 (6.2%)	NA - LN ^{*I}	0.10	9 (3.9%)	12 (8.3%)	NA - LN ^{*I}	0.10
Neurologic pain requiring treatment: Surgical (return to OR suture removal) ^a	0 (0.0%)	1 (0.9%)	NA ^{*2}	0.49	1 (0.4%)	2 (1.4%)	NA - LN ^{*I}	0.56
Midurethral sling mesh erosion/exposure at 4 weeks to 24 months	2 (1.7%)	1 (0.9%)	NA - LN ^{*I}	1.00	3 (1.3%)	1 (0.7%)	NA - LN ^{*I}	1.00
Vaginal cuff suture exposure at 6 to 24 months [‡]	15 (12.8%)	22 (19.5%)	0.4 (0.2, 1.1)	0.08	37 (16.1%)	24 (16.7%)	0.8 (0.4, 1.5)	0.42

No occurrences of urethral injury, rectal injury, or major vascular injury in women with advanced prolapse.

One woman with delayed recognition of ureteral injury also had intraoperative ureteral obstruction.

Unless otherwise noted below, models adjust for concomitant hysterectomy, surgeon, BPMT treatment assignment*, surgical assignment*, baseline POPQ severity* and all interactions between variables with an asterisk.

[#] Surgeon was removed from the model to achieve convergence.

^g 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)

^{*1} Result(s) not shown because of low numbers leading to low reliability of test. Unadjusted Fisher's exact test p-value reported.

^{*2} Unadjusted Fisher's exact test results shown because there are zero outcomes in one group