Int Urogynecol J
DOI 10.1007/s00192-017-3415-3

ORIGINAL ARTICLE

Self-retaining support implant: an anchorless system for the treatment of pelvic organ prolapse—2-year follow-up

Gil Levy[1] · **Anna Padoa**[2] · **Zoltan Fekete**[3] · **George Bartfai**[3] · **Laszlo Pajor**[3] · **Mauro Cervigni**[4]

Received: 14 March 2017 / Accepted: 26 June 2017

Abstract

Introduction and hypothesis The search for an improved vaginal mesh prompted the development of a new anchorless implant. The objective was to report on outcome after 2 years of a technique using a self-retaining support (SRS) implant.

Methods Patients with anterior vaginal wall prolapse, with/without apical prolapse, were recruited. Participants underwent surgical repair using the SRS device. Demographic data, pre-surgical Pelvic Organ Prolapse Quantification (POP-Q) scoring, quality of life (QoL) questionnaires (Pelvic Floor Distress Inventory Short Form 20 [PFDI-20], Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire 12 [PISQ-12]), and surgical data were collected. Patients were followed at 2 weeks, 2, 6, 12, and 24 months after surgery. Objective anatomical success was defined using the NIH criteria.

Results Twenty women were recruited for the study with an average age of 62.1 years and an average parity of 4.0 deliveries. Average BMI was 28. Pre-operative mean POP-Q measurements were Aa =1.40 (−1 to 3) cm, Ba = 2.3 (−1 to 6) cm and C = 0.4 (−7 to 6) cm. Surgical time averaged 31.2 min. Estimated blood loss averaged 165 ml. No intra-operative complications were observed. One case (5%) of frame erosion was documented 8 months after surgery. At 2 years' follow-up, mean POP-Q measurements were: Aa = −2.95 (−3 to −2) cm, Ba = −2.85 (−3 to −2) cm, and C point −6.90 (−10 to −3) cm. Seventeen (85%) patients had stage 0 and 3 patients (15%) had stage 1. No mesh erosions or chronic pelvic pain were documented at follow-up. The total PFDI score at follow-up was decreased by 92.8 points ($p < 0.0001$).

Conclusions At 2 years' follow-up, the SRS implant was found to be safe, showing no intra-operative or immediate post-operative complications. All women presented with POP-Q measurements of the anterior and apical compartment at normal value (Ba ≤ −2 cm) and statistically significant subjective improvement.

Keywords Pelvic organ prolapse · Vaginal mesh · Self-retaining support implant

Introduction

Despite providing good anatomical results compared with traditional native tissue repair, the use of vaginal mesh for the treatment of pelvic organ prolapse has been accompanied by more severe intra- and post-operative complications, such as organ perforation, bleeding, mesh erosion, mesh contraction, and pain [1, 2].

This rather high complication rate has led the FDA to publish public alerts in 2008 and 2011 (https://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm079028.htm, https://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm262435.htm). Clinical studies support

The surgical technique was presented as a video presentation at the 2015 IUGA meeting, Nice, France (https://www.youtube.com/watch?v=WT0V-WCeYkU). The abstract including preliminary data was presented as an e-poster at the 2016 IUGA meeting, Cape Town, South Africa

✉ Gil Levy
2gillevy@gmail.com

[1] Maynei Hayeshua Medical Center, 17 Povarski Street, Bnei Brak, Israel

[2] Asaf HaRofeh Medical Center, Tel Aviv, Israel

[3] Szeged University Hospital, Szeged, Hungary

[4] Catholic University, Rome, Italy

Published online: 14 July 2017

the conclusion that mesh-anchoring techniques are a major risk factor for complications with the current commercial mesh kits [3].

The search for the optimal solution for POP treatment is based on the need to imitate the natural physiology of the pubo-cervical fascia, providing the anatomical benefits of mesh implants, while eliminating the complications of current techniques. A review of the literature provides solid evidence that the anchoring techniques that accompany the placement of vaginal implants are a major factor in the occurrence of complications: organ perforation during the anchoring technique, unbalanced scar formation at the anchoring points, tension, folding, and contraction that can cause pain, dyspareunia, and failure leading to re-operation [3, 4].

For this purpose, a new concept involving an anchorless implant was developed. The assumption was that an anchorless neo pubo-cervical fascia would accurately mimic the physiological supporting system, therefore providing adequate level II support. Furthermore, extending the neo-fascia to the level of the sacrospinous ligaments would achieve additional level I support. The device was named after its fundamental concept, SRS, which stands for self-retaining support.

The purpose of this report is to describe the results of the "first in human" series of patients who underwent surgery using the SRS implant. The study was carried out after meticulous evaluation in animal and cadaver models [5].

Materials and methods

This is a prospective, multicenter, international study for the evaluation of feasibility, safety, and cure rate of POP surgery using the SRS implant. Approval was obtained from the relevant health ministries and local ethics committees in Israel and Hungary, before recruitment.

Patients with at least second-degree anterior compartment prolapse were recruited from the gynecology clinics in each participating hospital. All participants signed an informed consent, translated to the local language, after a detailed explanation of the risks involved in vaginal implants was provided. Exclusion criteria included: previous POP repair with mesh, age > 75 years old, Pelvic Organ Prolapse Quantification (POP-Q) scoring less than stage 2, or asymptomatic POP.

The device is composed of an ultra-light titanized polypropylene mesh (16 g/m^2) stretched and retained in place by a U-shaped flexible frame made of a biocompatible implantable polymer (Fig. 1). The SRS lateral arms have been designed to mimic the shape of the arcus tendinous fascia pelvis (ATFP). The arms are connected ventrally by a bridge designed to allow the passage of the urethra. The frame is composed of a solid, but flexible material. The frame functions as a mesh-retaining system by holding the mesh stretched under preload tension. Such tension prevents the mesh from bunching or contracting during the healing process. The shape of the device, which accurately imitates the anterior vaginal wall hammock, prevents mobilization and therefore no anchoring or fixation is required.

Fig. 1 The self-retaining support (SRS) implant

The surgical technique involves carrying out an anterior colpotomy and performing central dissection of the bladder from the vagina (Fig. 2). Dissection is then extended to the para-vesical space for direct bilateral palpation of the ischial spines. The surgeon can choose one of three implant sizes: small, medium and large. The difference among the sizes is the length of the lateral arms. The implant is positioned in place with no tension, with the arms not flexed and the mesh fully stretched. Should any tension be applied on the implant, the surgeon should remove the implant, extend the dissection area and re-insert or change the size of the implant. The device is inserted between the bladder and the vaginal mucosa with the lateral arms following the anatomy of the ATFP. The connecting bridge is positioned under the pubic symphysis. Appropriate location is confirmed by visualization of a symmetrically positioned device and a fully stretched mesh under the bladder. In the case of uterine preservation, the cervix is sutured to the proximal edge of the mesh. No other anchoring

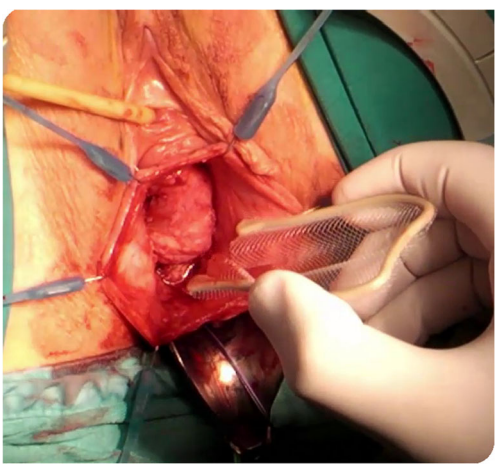

Fig. 2 Surgical insertion of the SRS

techniques are used. The vaginal incision is closed with no tension and vaginal packing is used for 24 h.

Demographic and background morbidity data, pre-surgical POP-Q scoring, and QoL questionnaires (validated Pelvic Floor Distress Inventory 20 [PFDI-20] and Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire 12 [PISQ-12]) were collected [6]. Objective anatomical success was defined as POP-Q stage 0 and 1 prolapse using the NIH criteria [7]. The PFDI-20 is divided to three domains: Pelvic Organ Prolapse Distress Inventory 6 (POPDI-6), Colorectal–Anal Distress Inventory (CRADI-8), and Urinary Distress Inventory (UDI-8). Each domain is calculated in a 100-point scale and all are added to a total score ranging from 0 to 300. Subjective success was defined as subjects having an improvement in POPDI/PFDI score that achieved the minimally important difference (MID). Total PFDI-20 was evaluated using an MID of ≥15 points per domain or a total score of 45 points. PISQ-12 score ranged from 0 to 48 and MID = 6. Surgical data included intra- and post-operative complications, time of surgery, and estimated blood loss. Postoperative data included vital signs, laboratory results, pain level, and length of hospital stay. Patients were followed at 2 weeks, 2, 6, 12, and 24 months after surgery. Objective and subjective primary end points were defined at 24 months.

Statistical analysis used the analysis of variance (ANOVA) test, where the null hypothesis is that all subgroup means are equal. Results of the two-way ANOVA on change of points Aa, Ba, and C by subject and visit were analyzed, looking at *P* values of the term visit in the model to evaluate statistical significance. Pre- and post-surgery POP-Q measurements were calculated using a nonparametric Wilcoxon signed rank test.

Results

Twenty women were recruited for the study. The first patient was enrolled in September 2014. The last patient completed her 24-month follow-up visit in February 2017. None of the patients withdrew from the study and none was lost to follow-up at 12 months. One patient did not consent to the extension of the follow up period (originally 12 months) and did not participate in the last follow-up visit (at 24 months). Table 1 describes patients' demographics. Eight patients were hypertensive and 2 were smokers. Pre-operative mean POP-Q measurements were Aa =1.40 (−1 to 3) cm, Ba =2.3 (−1 to 6) cm, and C = 0.4 (−7 to 6) cm. Nineteen (95%) patients suffered from both anterior and apical compartment prolapse, whereas one (5%) patient had only anterior prolapse.

All patients underwent transvaginal repair of anterior and apical compartment prolapse using the SRS. Five patients underwent concomitant vaginal hysterectomy for uterine abnormality and 5 had repair of the posterior compartment as well. Surgical time for the SRS implantation averaged 31.2 (21–50) min. Estimated total surgical blood loss averaged 205 (150–500) ml. Estimated blood loss for patients who underwent an implant-only procedure averaged 165 ml. No intra-operative complications were observed.

Table 1 Baseline demographic and clinical data

Variable	Value ($N = 20$)	SD
Mean age years (range)	61.95 (50–75)	6.58
Mean parity (range)	4.0 (1–16)	
Mean BMI (range) (kg/m^2)	28.13 (20.3–35.4)	4.28
Previous prolapse surgery	5 (26%)	
Previous hysterectomy surgery	3 (15%)	

Nineteen patients completed their 24-month follow-up visits. The overall mean follow-up period was 26.5 (range 24.7–29.6) months. Table 2 summarizes the anatomical out come at 2 years' follow-up. Seventeen patients (84.2%) had stage 0 prolapse and 3 patients (15.8%) had stage 1 prolapse. At 24 months' follow-up, significant anatomical changes were found in the points Aa (1.4 to −2.9 cm), Ba (2.3 to −2.8 cm), and C (0.4 to −7 cm). No cases of mesh erosion or chronic pelvic pain were documented at follow-up.

As for the subjective outcome, summarized in Table 3, PFDI scores showed significant improvement in both prolapse and urinary domains in addition to improvement in total scores. No deterioration was noted in the colorectal or the incontinence domains of the questionnaire.

Considering a standard MID of 15 points per domain and 45 points in total PFDI scores, results showed a significant improvement in the prolapse domain, incontinence domain, and total PFDI-20 scores. POPDI-6 (POP domain) showed a decrease of 41.94 points ($p < 0.0001$) at follow-up from baseline scores. The CRADI-8 (posterior compartment domain) scores were 14.5 points ($p = 0.0016$) lower at follow-up than at baseline and demonstrate no deterioration at the posterior pelvic compartment. The UDI-6 (urinary incontinence domain) showed a decrease of 36.3 points ($p = 0.0167$). The total PFDI score was decreased by 92.75 points ($p = 0.0001$).

Thirteen patients (65%) were sexually active during the study and 10 patients filled in the PISQ-12 questionnaire. Of these patients, 5 reported a nonsignificant improvement, 4 had a significant improvement, and 1 had a nonsignificant deterioration. Three patients who were inactive became sexually active after surgery. None of these patients reported dyspareunia. Two intra-operative cystoscopies were performed for minimal hematuria, with no bladder injury documented. Post-operatively, one patient received one unit of packed cells and no events of urinary retention were recorded. One patient developed de novo stress urinary incontinence, which was treated successfully with pelvic floor muscle training.

Table 2 POP-Q measurements at baseline vs 24 months' follow-up

Variable	Pre-operatively *n* (%)/cm ± SD (range)	24 months post-operatively *n* (%)/cm ± SD (range)	*P* value*
POP-Q			
Stage 0	0	17 (85%)	
Stage 1	0	3 (15%)	
Stage 2	7 (35%)	0	
Stage 3	5 (25%)	0	
Stage 4	8 (40%)	0	
Mean			
Point Aa (cm)	1.4 ± 1.5 (−1 to 3)	−2.95 ± 0.2 (−2 to −3)	0.000
Point Ba (cm)	2.3 ± 2.6 (−1 to 6)	−2.8 ± 0.3 (−2 to −3)	0.000
Point C (cm)	0.4 ± 3.5 (−7 to 6)	−7 ± 1.6 (−10 to −5)	0.000
TVL (cm)	7.55 ± 1.35 (5–11)	7.75 ± 1.07 (6–10)	0.519
Ap (cm)	−1.40 ± 1.98 (−3 to 3)	−2.15 ± 0.93 (−3 to 0)	0.18
Bp (cm)	−1.2 ± 2.89 (−3 to 6)	−2.0 ± 1.026 (−3 to 0)	0.569

Values given as mean ± SD (range)

*Nonparametric Wilcoxon signed rank test

One case (5%) of frame erosion into the anterior vaginal wall was documented 8 months following the procedure. The eroded part of the frame was resected under local anesthesia in an ambulatory setting. The patient's symptoms were relieved immediately after the resection. This was the only case where a large frame was used, which we hypothesize to have caused excessive pressure on the vaginal mucosa, causing the erosion.

Discussion

Our results suggest that the clinical use of the SRS implant for the treatment of anterior and apical vaginal wall prolapse might be safe and effective, with no intra- or immediate post-operative complications and optimal anatomical and subjective cure at 2 years.

According to data published by the FDA, most mesh complications are documented during the first 6 months following surgery and include organ perforation, bleeding, and mesh-related adverse events such as mesh erosion, mesh contraction, and pain. Twenty-four months' follow-up of the SRS was a sufficient basis for comparison with other mesh kits.

In comparison with reports on current available vaginal mesh kits, the safety profile and clinical outcome of the SRS implant seem significantly better: no mesh erosion, a single, preventable case of frame erosion (5%), no pain complications, and no negative impact on lower urinary tract symptoms. Intraoperative cystoscopy was performed in 2 patients for safety reasons. Routine cystoscopy should be considered, especially in concurrent prolapse surgery.

Furthermore, participating surgeons rated the implantation procedure as "easy." Although the present study was the first in-human clinical trial and represents the learning curve for the procedure, the operative time averaged only 30 min.

A recent publication by Huggele et al. [8] reported on the 2-year follow-up of 270 patients treated by transvaginal mesh for anterior and/or apical prolapse. The cohort included 95.2% pre-operative stage 3–4 anterior compartment prolapse. Reported outcome was of a 75.9% objective success rate for the anterior compartment at 1 year. Similar results reported by Azais et al. [9]. Data on complications included 7.5% rate of pain during pelvic examination at 1 year, 1.5% bladder injury, 11.1% buttock pain, 3% need for analgesic infiltration, and 7.8% post-operative voiding dysfunction. In our cohort of patients, there were no cases of pain or voiding dysfunction. None of our patients was re-operated for recurrent prolapse or

Table 3 QoL (Pelvic Floor Distress Inventory Short Form 20 [PFDI-20], Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire 12 [PISQ-12]) scores at baseline vs follow-up

Variable	*n*	Pre-operatively *n* = 20 (SD)	24 months *n* = 19 (SD)	Difference	*P* value
Total PFDI	19[a]	129.8 (61.59)	37.05 (62.17)	92.75	0.0001
POPDI-6	20	53.12 (26.8)	11.18 (19.15)	41.94	< 0.0001
CRADI-8	20	27.83 (23.55)	13.32 (23.98)	14.51	0.0258
UDI-6	20	48.88 (25.42)	12.54 (21.42)	36.34	0.0167
PISQ-12	9	29 (NA)	34 (NA)	5	NA

POPDI-6 Pelvic Organ Prolapse Distress Inventory 6, *CRADI-8* Colorectal–Anal Distress Inventory 8, *UDI-6* Urinary Distress Inventory 6

[a] One patient lost to follow-up at 52 weeks

stress urinary incontinence by the end of the first and second years.

Mesh contraction and bunching can cause nerve entrapment and excessive tension on the fixated mesh arms, which both lead to pain. It is documented that mesh folding and contraction is one of the reasons for chronic pelvic pain and dyspareunia. Partial removal of the mesh at the fixation points and reducing the tension on implanted mesh has been shown to resolve pain symptoms in 90% of patients [3]. It was shown that graft augmented colporrhaphy (mesh reinforced native-tissue repair) and other non-fixation mesh techniques, cause less pelvic pain [10].

Current mesh kits provide a stand-alone mesh that is fixated at four corners in the pelvis. Although this is stressed by all manufacturer's instructions and training programs, current securement techniques do not ensure that the mesh is placed in a tension-free, flat, nonfolded fashion. Even when anchoring the mesh to four corners in a flat and tension-free configuration, there is no guarantee that dynamic pressures and scar accumulation construction forces will not cause mesh contraction and folding over time.

The SRS solid frame provides a long-term reassurance from mesh contraction and bunching.

Mesh erosion is probably the most common complication of surgery with the current mesh kits, with a reported incidence of 10.3% in a large meta-analysis [11] and of 12.2% in the latest Cochrane review on POP surgery [12]. We believe that elimination of mesh folding and bunching may reduce exposure through the vaginal incision and may lead to a lower mesh erosion rate.

Margulies et al. [4] identified mesh folding in 9 out of 13 patients suffering from vaginal mesh exposure. Mesh folding has been suggested as an important contributing factor in mesh exposure, secondary to local inflammatory reaction and interference with the healing process at the incision site.

The high exposure rate reported with past commercial kits has possibly been decreasing due to the current use of lightweight polypropylene mesh, which seems to reduce inflammatory reaction and mesh shrinkage [13]. Beyond containing ultralight polypropylene (16 g/m^2), the SRS mesh contains titanium ions, which may have contributed to the low mesh erosion rate seen in our cohort [14].

Anchoring the mesh to four corners in a flat and tension-free configuration does not prevent mesh contraction and folding over time. The SRS solid frame precludes mesh contraction and bunching.

In this clinical trial, there were no mesh erosions and only one case of frame erosion, which occurred secondary to application of a large device, and it was treated with good results. We believe that this adverse event could easily be prevented by the use of a smaller frame size and adequate dissection. Regarding dyspareunia, patients who were sexually active and completed the PISQ-12 questionnaire did not report dyspareunia, but we were unable to reach any conclusion owing to the small cohort.

A weakness of this study is that the physicians involved were not blinded to the anatomical results and the surgeons did perform post-operative POPQ measurements follow-ups on their own patients, potentially biasing the results. However, the main limitation of this study is the limited sample size of patients included so far. We are now carrying out a 3-year follow-up study on the efficacy and safety of the SRS device in a larger patient population.

In conclusion, POP repair using the SRS anchorless implant seems a very promising alternative surgical solution for advanced anterior and apical compartment prolapse. A larger sample size and longer follow-up is required to strengthen and confirm our conclusions.

Compliance with ethical standards

Conflicts of interest Gil Levy MD is the inventor of the device and a shareholder in Lyra Medical Ltd. None of the other authors has any financial disclaimer or conflicts of interest.

Funding The research was funded by Lyra Medical Ltd., Makura Farm, Israel.

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