Self-Retaining Support (SRS) Implant: a Neo-Pubocervical Fascia - Anchorless System for the Treatment of Advanced Pelvic Organ Prolapse – Report of 70 Patients

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Abstract

Introduction: The search for an improved trans-vaginal treatment prompts the development of a new anchorless implant for the treatment of advanced anterior vaginal wall prolapse with or without apical prolapse.

Objective: To report on the safety and up to three years follow-up clinical outcome of an innovative technique using a self-retaining support implant (SRS) for the treatment of advanced anterior vaginal wall prolapse with or without apical prolapse.

Methods: Two multicenter, international studies for the evaluation of safety and three years follow-up clinical outcome of patients treated surgically for anterior vaginal wall prolapse using a self-retaining support implant (SRS).

Results: Seventy women underwent surgical repair using the SRS. Up to 36-months follow-up results showed no intra-operative or immediate post-operative complications. One patient (1.4%) had a symptomatic recurrence of her apical prolapse (C=0), two patients (2.8%) had an asymptomatic recurrence of their apical prolapse, representing 94.3% anatomical success.

Conclusion: The results of these studies show a reassuring safety profile, excellent clinical outcome and ease of procedure. We conclude the SRS implant is a promising surgical technique for the repair of advanced anterior vaginal wall prolapse with or without apical prolapse.

Introduction

Pelvic Organ Prolapse (POP) is a common condition among women which is described as the protrusion of pelvic organs through the vaginal opening. POP is caused due to damage to the pelvic organs' supporting structures such as ligaments, fasciae or muscles[1]. Studies showed that symptomatic POP should be treated with surgical reconstruction of the connective support structures. Surgeons and bio-engineers developed various techniques, focusing on the repair of the damaged connective tissue supporting components.

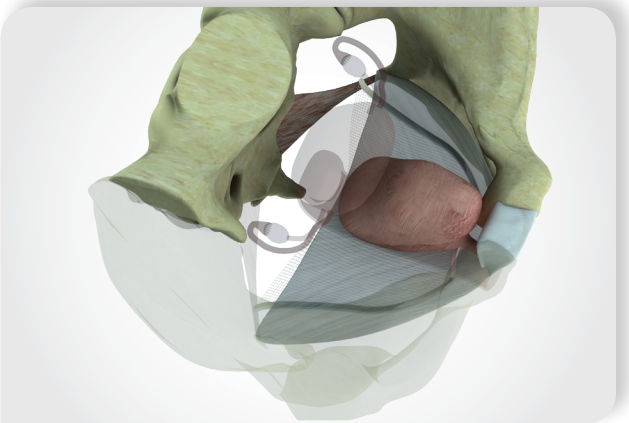

Figure 1 - SRS location - top view

Structures that support the pelvic organs were described by DeLancey who distinguished between three levels of pelvic support. Based on this understanding, surgical techniques were developed aiming at the restoration of each level of support separately, i.e. site specific repair. Traditionally, damage to level II support in the anterior compartment was repaired by approximation of the remnants of the pubocervical fascia, using absorbable suture material, i.e. anterior colporrhaphy. This technique and its multiple modifications lead to a wide range of reported anatomical success rates.

The introduction of synthetic materials augmenting or replacing the damaged connective tissue provided better restoration of level II support and lead to improved anatomical results. Simultaneously, several publications showed that restoring apical (level I) support is a cardinal factor in the surgical success rate. Following this understanding, implant anchoring techniques were modified in order to provide a solution supporting both level I and II. This was done by extending the mesh fixation points towards the sacrospinous ligaments. The use of vaginal mesh has been found to provide good anatomical results compared to traditional native tissue repair, however, it has raised concern due to higher intra - and post-operative complications, including organ perforation, bleeding, mesh erosion, mesh contraction and pain[2,3]. Clinical studies support the conclusion that mesh anchoring techniques may be the main reason for the complications encountered with current mesh kits. Regulatory authorities such as the FDA issued alerts on vaginal mesh complications in 2008 and 2011[4], consequently surgeons reduced the use of vaginal meshes. Native tissue repair (NTR) and sacrocolpopexy became the preferred approaches for POP repair although their long-term success rates are not optimal[5].

For the purpose of keeping the benefits of mesh implants while eliminating complications of current techniques, a new concept involving anchorless placement of an implant was developed. The assumption was that accurately imitating the physiologic supporting structures, by creating an anchorless neo pubocervical fascia will provide adequate level II support reconstruction. Extending the depth of the device to the level of the sacrospinous ligaments provides additional level I support. The device was named after its fundamental concept: **SRS**, which stands for **Self-Retaining Support**.

In September 2014, the first-in-women SRS-I study was initiated in women with advanced symptomatic anterior vaginal prolapse with or without apical involvement. This was made possible by previous meticulous evaluation in animal and cadaver models and by obtaining the appropriate regulatory approval for human clinical studies.

A second study, the SRS-II, was initiated on 2016, for additional safety and efficacy evaluation.

The purpose of this manuscript is to report on three years safety and efficacy of the SRS technique for

the treatment of advanced anterior vaginal wall prolapse, with or without apical prolapse.

Study design and methods

Two prospective, multi-center, international studies were conducted at four centers in Israel and Hungary. Approvals by the local ethical committees were obtained prior to patients' recruitment. All patients signed an informed consent form, translated into their local language, after receiving a detailed explanation of the risks involved with vaginal implants. The initial research protocol included 20 patients with one-year follow-up, which was extended to 36 months. Following the results of this study, a second protocol was initiated with additional 50 patients. Both studies protocols were similar and results were combined for this report. Symptomatic patients with at least 2nd degree anterior compartment prolapse with or without apical prolapse were recruited. Exclusion criteria included previous vaginal mesh surgery or age >75 years old.

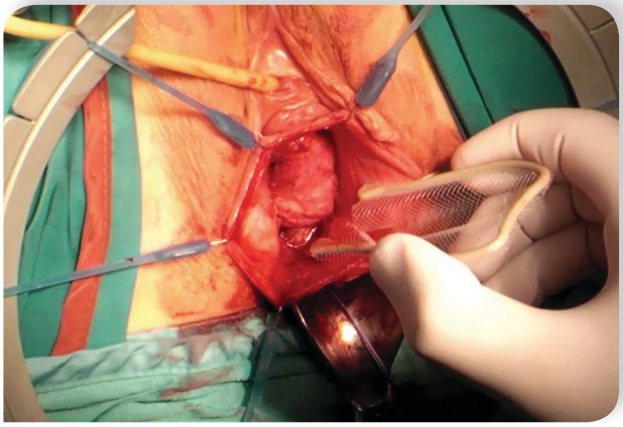

Figure 2 - SRS Insertion

In both studies, demographic and background morbidity data, pre-surgical POP-measurements and validated QoL questionnaires (PFDI-20, PISQ-12) were collected. Peri-surgical data included intra-operative and post-operative complications, length of the procedure and estimated blood loss. Postoperative data included vital signs, lab results, pain level (measured using VAS scale) and length of hospital stay. Patients were invited for the follow-up visits at 2 weeks, 2, 6, 12, 24 and 36 months post-surgery. The follow-up includes anatomical and subjective evaluation. Adverse events were/are collected through the entire study duration.

The implant and surgical technique

The implant is comprised of polypropylene mesh stretched within a solid flexible frame. The ultra-light titenized mesh (16 gr/m^2) is stretched and retained in place by a U-shaped structure. The surgical technique includes central dissection of the bladder from the vagina, which extends to the paravesical space for direct bilateral palpation of the ischial spines. The device is inserted between the bladder and the vaginal mucosa with the lateral arms following the anatomy of the arcus-tendineus-fascia-pelvis (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 case of uterine preservation, the inner aspect of the upper cervical lip is sutured to the middle of the proximal edge of the mesh. No other anchoring techniques are used. The vaginal incision is closed with no tension and vaginal packing is used for 24 hours.

Results

The first patient was enrolled on September 2014. The last patient from the first study completed her last follow-up visit (36 months) on March 2018. The second study was initiated in March 2018 and will follow the patients for 3y post-op until the end of August 2020. One patient did not consent the extension of the follow-up period (originally 12 mo.). This patient reported no Adverse Events, no symptoms and no other changes from her previous (12 mo.) follow-up visit.

Table 1 describes the patients' demographic data. Average age was 63.0 (43-79) years old, average parity was 4.6 (1-16) deliveries, 6 patients had previous vaginal surgery and 6 had prior hysterectomy. Average BMI was 27.0 (20.3-36.6) Kg/m^2, 28 patients had hypertension, 15 were diabetic and 10 were smokers. Pre-operative POP-Q was Aa = 2.0 (-1 to 3) cm, Ba =3.1 (-2 to 6)

cm and C=0.4 (-8 to 6) cm. Sixteen (23%) patients had isolated anterior wall prolapse (C<-1cm).

Variable	Value (N=70)
Mean Age [years]	63.0 (43-79)
Mean Parity [# of childbirth]	4.6 (1-16)
Mean BMI [kg/m^2]	26.3 (20.3-36.6)
Previous prolapse surgery	6 (8.6%)
Previous Hysterectomy	6 (8.6%)

Table 1. Baseline demographic and clinical data

As of August 2019, twenty-seven patients completed their 36 months follow-up, 33 patients completed their 24 months follow-up, 10 patients completed their 12 months follow-up. The overall mean follow up period was 27.7 months (range 11.4-41).

All patients underwent transvaginal repair of anterior and apical compartment prolapse using the SRS. Ten patients underwent concomitant vaginal hysterectomy, fourteen patients had concomitant midurethral sling and fifteen had repair of the posterior compartment as well. Surgical time for the SRS implantation averaged 24.7 min (10-50 min). Estimated total surgical blood loss averaged 155 ml (25-500 ml). No intra-operative complications were observed.

Two intra-operative cystoscopies were performed for minimal hematuria with no bladder injury documented. Post-operatively, one patient received one unit of packed cells. One patient experienced voiding dysfunction approx. 12 months post procedure which was recorded and resolved by resecting the bridge of the SRS-frame under local anasthesia in an ambulatory surgical procedure. The patient was discharged on the same day and reported relief of symptoms at FU. Two events of de novo SUI were reported and treated with a mid-urethtral sling under regional anesthesia.

One case of 1 cm frame erosion into the anterior vaginal wall was documented 8 months post-operatively. The eroded part of the frame was resected under local anesthesia in an ambulatory setting. Patient's symptoms were relieved immediately after the resection, and she remained asymptomatic at the 12-month, 24-month and 36 months visits. This was the only case where a large sized frame (out of three sizes that are available to the surgeon) was used and may have caused excessive pressure on the vaginal mucosa that lead to the erosion.

Table 2 presents the results assuming a composite objective (Ba ≤ 0 and/or C ≤0), subjective (PFDI-20 Q3 ≤2), and retreatment success criteria.

Note: where the measurement of point C was lower than point D by more than 4 cm (i.e. D-C≥4), it was considered as Cervix Elongation, and point D was used for prolapse staging.

Variable	Results
Composite success	98.6% (69/70)
Objective success	98.6% (69/70)
Anterior compartment	100% (70/70)
Apical compartment	98.6% (69/70)
Subjective success	98.6% (69/70)
No retreatment for POP	98.6% (69/70)

Table 2. Study results according to recent FDA's 522\PMA studies' end-points

At the last follow up visit for each patient, 94.3% showed anatomical success with POP-Q measurements. One patient (1.4%) had a symptomatic recurrence of her apical prolapse (C=0), and two patients (2.8%) had an asymptomatic recurrence of their apical prolapse. (Table 3). One patient (1.4%) required a re-surgery of recurrent apical prolapse. This patient presented with a cervix elongation that reached 1 cm below the hymen (C=1), 2 years post surgery. Patient underwent vaginal hysterectomy without any further prolapse treatment. No mesh erosions or chronic pelvic pain were documented at follow up.

Variable	Baseline	Post-Operative
POP-Q:		
Stage 0	0	57 (81.4)
Stage 1	0	9 (12.8%)
Stage 2	7 (10%)	4 (5.7%)
Stage 3	51 (73%)	0
Stage 4	12 (17%)	0
Point Aa	2.0 (-1 to 3)	-2.9 (-1 to -3)
Point Ba	3.1 (-1 to 6)	-2.8 (-3 to -1)
Point C	0.4 (-8 to 6)	-7 (-10 to 1)

* Values given as # of patients (%), mean cm (range)

Table 3. POP-Q measurements at baseline vs. last follow-up visit for each patient [N=70]. As of August 2019: 27 patients (39%) completed their 36 months FU; 33 patients (47%) completed their 24 months FU; 10 patients (14%) completed their 12 months FU;

PDFI-20 questionnaire results were analyzed using standard Minimally Clinically Important Difference (MCID) of 15 points per domain and 45 points in total PFDI scores. Results in table 4 show significant improvement in the prolapse domain, incontinence domain and total PFDI-20 scores. Combined results from both studies for the last FU visit that patient attended (i.e. 36/24/12/6 months FU) show the following: Pelvic Organ Prolapse Distress Inventory 6 (POPDI-6) decreased in average by 29 points. The Colorectal-Anal Distress Inventory 8 (CRAD-8) scores were an average 6.8 points lower at follow-up than baseline and demonstrate no deterioration at posterior pelvic compartment. Urinary Distress Inventory 6 (UDI-6) showed an average decrease of 23.2 points and total score was decreased by an average of 58.0 points.

Variable	Baseline	last FU visit	Diff.
POPDI-6	41.4	12.4	29.0
CRAD-8	24.1	17.2	6.9
UDI-6	40.3	17.9	23.1
Total	105.8	47.5	58.0

Table 4. combined QoL (PFDI-20) scores at baseline vs. last FU visit patient attended and completed the QoL (N=69)

Due to the intimacy and relevance nature of the PISQ-12 questionnaire questions, only 38 patients (54%) have provided enough data for analysis. This PISQ-12 low compliance rate provided limited data which was not enough for a valid and reliable conclusion. Nevertheless, available data showed no de-novo dyspareunia and an improvement in sexual function, although this improvement was not found to be clinically significant.

Discussion

The use of mesh in vaginal surgery for the treatment of pelvic organ prolapse (POP) has been found to provide good anatomical results, however it is accompanied by higher intra- and post-operative complications which include organ perforation, bleeding and mesh related adverse events such as mesh erosion, mesh contraction and pain[6,7]. The rate of secondary operations due to mesh complications have been reported in 1 out of 10 patients with mesh-augmented repairs[8]. Literature supports the conclusion that mesh fixation is the main reason for complications with current transvaginal mesh techniques.

It is documented that mesh folding and contraction is one of the reasons for chronic pelvic pain and dyspareunia[9]. Mesh contraction and bunching can cause nerve entrapment as well as excessive tension on the fixated mesh arms, which both lead to pain. 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[10].

Elimination of mesh folding and bunching may also reduce exposure through the vaginal incision and may lead to a lower mesh erosion rate. Margulies et al., identified mesh folding in nine out of 13 patients suffering from vaginal mesh exposure[11]. It is believed that mesh folding might be an important contributing factor in mesh exposure secondary to local inflammatory reaction and interference with the healing process at the incision site[12].

Current mesh kits provide a standalone mesh that is fixated at four corners in the pelvis. These

implantation and securements techniques do not assure that the mesh is placed in a tension-free, flat, non-folded fashion. Even when placing and anchoring the mesh in a flat and tension free configuration, there is no guarantee that dynamic pressures and scar accumulation will not cause mesh contraction and folding over time. Moreover, considering the new adopted success criteria, where success is defined at the hyman level, the anatomic success rates for POP surgery using mesh is comparable to the success rates of native tissue repair, while patients are still exposed to mesh related complications and potentially retreatments[13].

Lyra has developed the SRS device to address these issues by designing an anchorless mesh product that is secured to a frame, allowing for the mesh to remain flat and tension-free during the tissue remodeling process.

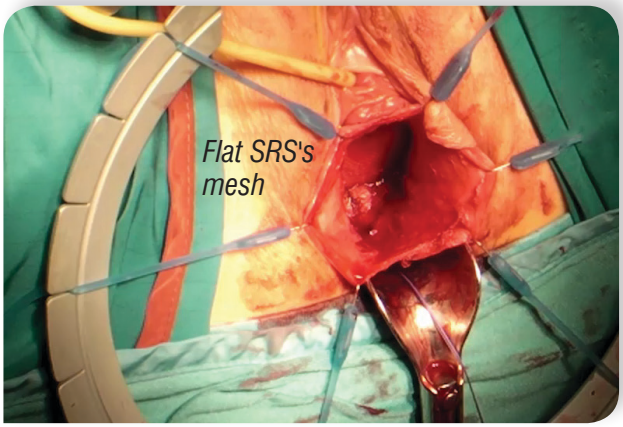

Figure 3 - Implanted SRS frame retains a flat, tension-free mesh

Creating a replacement of the damaged pubocervical fascia requires accurate imitation of the physiologic shape and attachment of this unique structure. The pubocervical fascia is stretched between the arcus-tendineus-fascia-pelvic (ATFP) on both sides of the pelvic wall along the interior surface of the internal obturator muscles. The distal attachment is located at the inner aspect of the pubic bone with an opening to allow the passage of the urethra. The SRS design follows these characteristics. Its lateral arms designed with the shape of the ATFP and are connected ventrally by a bridge designed to allow the passage of the urethra. This design was developed and tested in a series of experiments in cadaver model. The position of the arms was also investigated in order to assure that the solid frame does not create any pressure on vital structures in the pelvic floor and that they are located within a safe distance from major nerves and vessels in the pelvis. The innovative concept of the solid frame functions as the mesh retaining system and allows the use of ultra-light mesh (16 gr/m^2). The frame retains the mesh tension and thus prevents it from bunching or contracting during the healing process. This unique design eliminates bunching and folding, uneven scar formation and contracting under pressure that can cause complications. The device's shape prevents its mobilization and therefore no anchoring or fixation is required.

The neo pubocervical fascia allows repositioning of the bladder to its physiologic location accommodating for intra-abdominal pressure dynamics.

Conclusion

Results suggest that eliminating mesh fixation can potentially reduce both intra and post-operative complications.

The clinical use of this anchorless implant revealed no intra-operative or immediate post-operative complications and very high rate of anatomical and subjective cure at three-year follow-up. The sole case of frame erosion was secondary to an oversized implant and therefore can be easily prevented.

The SRS technology was developed to eliminate the high complication rate associated with anchored vaginal mesh kits and improve the low success rate associated with native-tissue repair. Lyra's SRS solution was proven in clinical trials to deliver exceptional safety and long-term efficacy.

Results suggest that the safety profile and clinical outcome of an anchorless implant is potentially better than that reported for other trans-vaginal surgical meshes. Out of 70 patients, only one case (1.4%) documented with frame erosion 8 months following the procedure. An investigation revealed

that this patient was the only one implanted with a larger size implant. Following this event, Lyra Medical decided to discontinue the use of various sizes and since then there were no recurrences. In another case, a patient complained of a slow urinary stream. Although objective tests found the mesh and the frame to be in a normal position in relationship to the urethra, the patient underwent a partial frame resection.

No other device related Serious AEs occurred.

The solid frame allows an anchorless surgical technique, assures long-term safety, retains the mesh at the desired location and provides the required long-term mechanical support. Although these studies demonstrate very convincing results, a confirmation is required including a larger sample size and a longer follow-up for a sufficient clinical evaluation for this new anchorless support concept to treat POP.

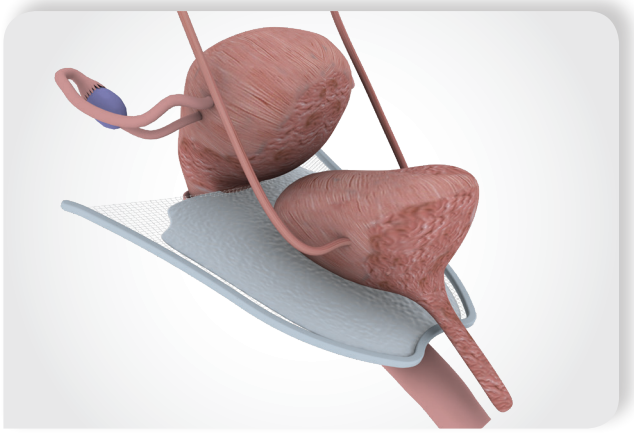

Figure 4 - Accumulated scar tissue provides level I & II support

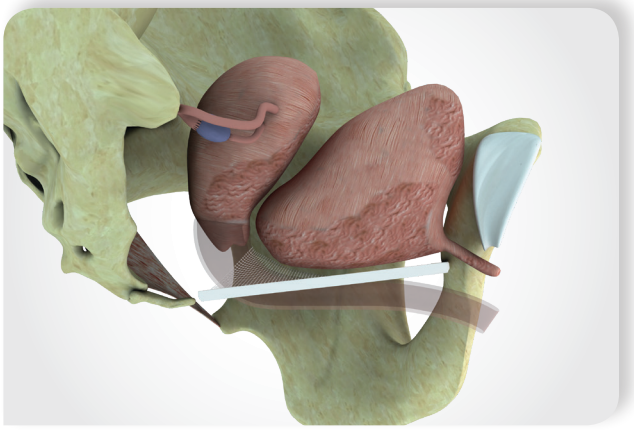

Figure 5 - SRS anatomical location

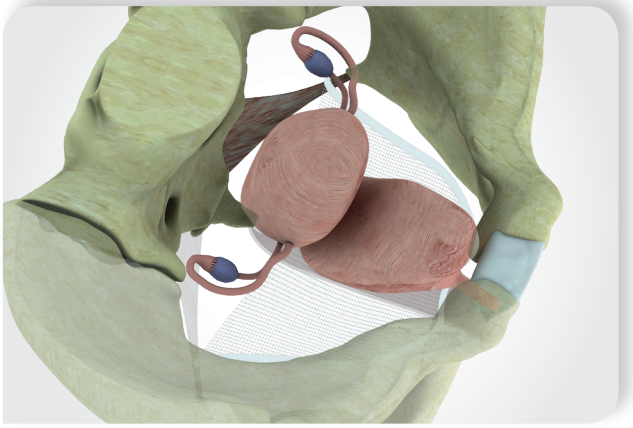

Figure 6 - SRS's arms follow ATFP anatomy

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