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STRESS INCONTINENCE AND PROLAPSE (S REYNOLDS, SECTION EDITOR)

Management of Recurrent Stress Urinary Incontinence After Failed Mid-Urethral Sling Placement

Philip A. Fontenot Jr[1] · Priya Padmanabhan[1]

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Abstract

Purpose of Review Our objective is to review the current literature on recurrent stress urinary incontinence after mid-urethral sling placement, focusing on evidence-based management considerations for this complex clinical problem.

Recent Findings Conservative, minimally invasive surgical therapies are currently available for management of persistent or recurrent SUI after a previous mid-urethral sling (MUS).

Summary Our review of the literature does not show a clear benefit of one approach over others and emphasizes that the ideal management for these complex patients should be determined using an individualized approach with a detailed discussion of patient symptoms, past surgical history, and goals. For symptomatic patients who are surgical candidates and desire intervention, trans-urethral bulking agents, repeat retropubic (RP) MUS, or salvage autologous pubovaginal (PV) sling appear to be the most well-described management strategies.

Keywords Urinary incontinence · Mid-urethral sling · Pubovaginal sling · Sling failure

Introduction

Stress urinary incontinence (SUI) represents a prevalent and frustrating diagnosis for both patients and physicians in the United States (USA) with an estimated lifetime prevalence ranging from 4 to 35% and affecting greater than 50% of patients with urinary incontinence [1, 2]. SUI is defined as the unintentional loss of urine caused by physical activity and/or movement such as coughing/sneezing/lifting. Depending on bother, severity, and goals of care, SUI is often initially managed with conservative measures like pelvic floor exercises (PFRT), with minimally invasive and surgical therapies being offered to those who do not respond to conservative treatment [3, 4].

In the USA, mid-urethral slings (MUS) are considered the gold standard procedure for treating SUI that is refractory to conservative measures and have long-term cure rates of 77–90% [4]. Nevertheless, while the initial management of SUI has a clear evidence-based treatment algorithm progressing from conservative to more invasive approaches, the management of recurrent SUI after a previous incontinence procedure, specifically a previous MUS, remains controversial with a paucity of evidence available to help guide additional treatment recommendations [5, 6••, 7•]. Furthermore, since it has been shown that 8.6–17% of patients with SUI require additional procedures for SUI management due to either persistent or recurrence of SUI, an evidence-based algorithm for management of recurrent SUI is crucial [1, 8, 9]. Thus, our objective is to review the current literature on persistent or recurrent stress urinary incontinence after mid-urethral sling placement, focusing on evidence-based management options for this complex clinical problem.

Methods

A systematic review was conducted of the current available literature using a combination of the search terms "sling," "mid-urethral sling," "stress urinary incontinence," "recurrence," and "failure" in Pubmed, which resulted in 427 articles. Articles were screened by one reviewer for their relevance to our objective. Pertinent articles were reviewed in

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✉ Priya Padmanabhan
ppadmanabhan@kumc.edu

[1] Department of Urology, University of Kansas Health System, 3901 Rainbow Blvd. MS 3016, Kansas City, KS 66160, USA

detail and included in this review article with a preference given to articles being published in the last 5 years. Also, the reference section of all pertinent articles was also reviewed to help identify additional articles that discussed the management of recurrent SUI after previous MUS placement.

History of SUI Surgical Management

Historically, the Burch colposuspension was considered by many to be the gold standard surgical treatment for SUI. Over the past two decades, however, slings have gained significant popularity for SUI management in the USA due to reports of shorter recovery and comparable efficacy to the Burch procedure [6••]. Specifically, the Stress Incontinence Surgical Treatment Efficacy (SISTeR) Trial was a randomized controlled trial which compared the Burch procedure to autologous fascial pubovaginal slings (PVSs) and demonstrated not only a higher treatment success rate after PVS, but also a greater risk of post-operative voiding dysfunction [10]. Furthermore, in 2010, Novara et al. conducted a meta-analysis comparing the Burch colposuspension, pubovaginal sling, mid-urethral retropubic sling (RP), and trans-obturator sling (TO), which showed higher continence rates with slings than the Burch procedure, with the cost of increased intra-operative complications among slings [11]. Also, Zimmern et al. examined the SISTeR and Trial of Mid-urethral Slings (TOMUS) trials and found 5-year retreatment-free survival rates (and their standard errors) of 87% (3%), 96% (2%), 97% (1%), and 99% (0.7%) for the Burch, autologous fascial sling, trans-obturator MUS, and retropubic MUS groups respectively, indicating that slings have lower retreatment rates for recurrent SUI than the Burch procedure [7•].

Despite their high success rate and lower retreatment rates, MUS placement is not without complications. In a study of 363 RP slings, bladder injury was reported in 4.2%, de novo urgency in 5–20%, voiding dysfunction in 4–16%, UTI in 5.9–13%, bleeding in 1.7–6.7%, and urinary retention in 10% of patients [3]. Furthermore, TO slings, while thought to have a decreased risk of bladder injury and voiding dysfunction compared to RP slings, are known to have an increased risk of pain and nerve injury.

When comparing the two main types of MUS, trans-obturator (TO) and retropubic (RP), a recent Cochrane review looked at 55 trials encompassing 8652 women with SUI and reported on short-, medium-, and long-term subjective cure rates for each group. Specifically, the review found no difference in subjective cure rates between TO and RP MUS despite short-, medium-, and long-term follow-up, with subjective cure rates reaching as high as 98% in some studies [12]. In 2017, Novara et al. updated their 2010 meta-analysis, confirming their previous findings and suggesting that MUS are "more effective" than older procedures for SUI like the Burch colposuspension. The 2017 update also compared TO and RP MUS and demonstrated higher subjective and objective cure rates for the RP MUS, but at the cost of more complications and voiding dysfunction. Also, it showed that the efficacy of inside-out and outside-in techniques of TO MUS was similar, with a lower risk of vaginal perforation in the inside-to-out TO MUS placement technique [13•].

Recurrent SUI After Previous Incontinence Surgery and MUS Failure

Currently, there is no clear definition of MUS failure in the literature [6••]. In fact, definitions of sling failure are quite variable, with studies lacking consistency in how they define both objective and subjective successes/failures of slings. This variability represents one of the many challenges one faces when attempting to draw conclusions from the literature [6••]. Current examples of sling failure definitions include, but are not limited to, the following: (1) persistence of bothersome SUI measured subjectively; (2) cure of SUI with the emergence of de novo lower urinary tract symptoms (LUTS); (3) failure to cure SUI objectively; (4) emergence of de novo LUTS; and (5) post-operative complications (pain, erosion, urinary retention) [6••]. In addition, the timing of SUI after a previous MUS can affect whether or not the SUI is defined as a MUS failure or simply recurrence of SUI, with some considering an MUS failure only if SUI symptoms recur < 12 months after MUS placement. SUI recurrence without considering it a MUS failure has been argued by some if SUI returns > 12 months after MUS placement [14].

MUS has a surgical failure rate at 5-year follow-up ranging from 8 to 57%, which is quite variable [6••]. One study reported that 5–20% of patients undergoing MUS experience persistent or recurrent SUI, which is regarded as surgical failure [15]. Furthermore, Zimmern et al. found that half of women who were re-treated for recurrent SUI in the SISTeR and TOMUS trials were re-treated within the first year following their original procedure [7•]. Regardless, SUI after MUS is common and occurs within the first post-operative year in most cases.

Kavanagh et al. in their review of MUS failures were able to identify four main categories of failure in the literature [6••]. First, they describe "preoperative selection of high-risk patients" and reference Richter et al.'s study of 600 patients, reporting that patients with previous incontinence surgery, higher pad weight, older age, and maximal Q-tip excursion < 30 degrees were at higher risk for MUS failure within 1 year of surgery [16]. Second, they discuss "failure to correctly treat the original diagnosis," citing Holmgren et al.'s retrospective review of 760 patients treated with RP MUS, demonstrating cure rates in 85% of patients with pure SUI, compared to only 30% of those with mixed urinary incontinence (MUI) [17].

The remaining two categories include "new post-operative voiding dysfunction" and "failure of surgical technique" [6••, 12].

When the physician is concerned for MUS failure in a patient, a complete incontinence work-up is warranted and is the practice of the authors. This practice includes a complete history and physical examination that elucidates subjective data, including the severity of the incontinence, degree of bother and chronology of prior surgery, and the current symptoms. Furthermore, physical examination should be carried out with a full bladder in the dorsal lithotomy and/or standing positions to assess for objective incontinence with Valsalva. A complete speculum should also be used to assess for mesh erosion. Lastly, the urethra should also be visualized to assess for hypermobility, as SUI with an immobile urethra is suggestive of intrinsic sphincter deficiency (ISD). Other factors to consider are patient goals of care, assessment of a voiding diary, review of structured incontinence questionnaires to assess symptom severity, post-void residual volume, cystoscopy to rule out urethral erosion, urodynamic studies to document SUI, assessment for bladder outlet obstruction, sensory urgency and detrusor overactivity, and in some cases trans-vaginal ultrasound to help localize mesh. It should be noted that establishment of patient goals of care remain one of the most important factors to consider when deciding on the treatment of MUS failure, which the authors will discuss later in this manuscript. This in-depth evaluation of the patient with likely MUS failure has been advocated for in the literature by Kavanagh et al., as the cause of failure sometimes can be difficult to untangle [6••].

After completing a detailed evaluation, if a patient has pure SUI after a previous MUS placement, the SUI is caused by either persistent hypermobility or ISD, with ISD being the most likely cause of persistent or recurrent SUI after MUS [18]. Persistent hypermobility can be elicited on physical exam, while ISD is seen with a fixed urethra on exam in conjunction with an abdominal leak point pressure (ALPP) < 60 mmHg on urodynamic evaluation [18]. As we will discuss later, management options for a patient with SUI due to hypermobility will differ when compared to a patient with SUI due to ISD.

Management Options for MUS Failure

Non-surgical Conservative Therapy

Pelvic Floor Physical Therapy

For the poor surgical candidate or patient wishing to avoid additional surgical procedures for SUI, conservative management may be the best alternative. Pelvic floor physical therapy (PFRT) to strengthen the pelvic floor is often recommended as first-line therapy for recurrent SUI after previous surgical management, despite poor evidence that it is successful in this particular patient population [3]. Nevertheless, PFRT has had some success in patients with very mild SUI after a previous surgery for SUI [3, 18].

Medical Therapy

Off-label use of imipramine is another non-surgical option that has been historically prescribed to help with recurrent SUI due to its sympathomimetic effect to increase tone of the intrinsic sphincter. However, more recently, routine use of imipramine has fallen out of favor due its cardiac side effects [18].

Incontinence Pessary

A third, non-surgical management option is the use of an incontinence pessary like Uresta© or Impressa© to coapt the urethra and prevent leakage. It is important to note that while these agents are not approved for management of recurrent stress urinary incontinence after a previous surgical procedure for SUI, providers often use them anecdotally to manage recurrence. Patients often find these treatment options only mildly successful in the setting of surgical failure, when compared to more invasive management options [6••]. In conclusion, non-surgical options are available for management of SUI after previous surgical management, although rarely used, and may be a reasonable consideration for poor surgical candidates, patients who refuse additional surgery, or patients with mild SUI who desire a non-surgical approach.

Minimally Invasive Surgical Therapy

Trans-urethral Bulking Agents

The use of trans-urethral bulking agents is appealing to many patients due to their low morbidity, minimally invasive approach. However, they are often only a temporary solution to the problem and do not have good long-term outcomes, especially in the setting of MUS failure [6••, 18]. Kim et al. conducted a retrospective review of 56 patients treated with Durasphere for recurrent SUI after a previous MUS and reported a success rate (one or less SUI episode per week or 70% patient-perceived improvement) of only 40% at 5 years with an average follow-up of 64.3 months [19]. Gaddi et al. found a similar, poor outcome in their evaluation of 67 patients in the Kaiser database who had a previous MUS and developed recurrent SUI, reporting a 38.8% failure rate of bulking agents in their cohort [20]. Furthermore, a systematic review conducted by Nikolopoulos et al. in 2015 demonstrated a success rate of 38% for urethral bulking agents in the setting of SUI after a previous surgical procedure [21••]. Interestingly, Lee et al. conducted a retrospective study of 23

patients who received a bulking agent after failed MUS and reported a 77% patient satisfaction rate, despite only a 34.8% objective cure rate at 10-month follow-up, advocating for the use of bulking agents to treat patients with MUS failure [22]. Thus, the current literature suggests that trans-urethral bulking agents are an acceptable option for management of SUI in the MUS failure population, especially in poor surgical candidates, elderly patients, those wanting to avoid major surgery, and those with factors that would make more invasive options difficult if not impossible.

Sling Plication

Sling plication after failed MUS has been shown to have an acceptable success rate. In their evaluation of 20 women with recurrent SUI after MUS placement who underwent sling plication, Patterson et al. reported an overall subjective cure rate of 65%. Notably, sling plication cure rates differed between RP slings (88%) and TO slings (45%), but this difference was not statistically significant ($p = 0.07$) [23]. Feyeux et al. evaluated 19 patients with SUI after MUS treated with plication and reported a 73.7% subjective cure rate with an additional 10.3% reporting subjective improvement in symptoms despite not achieving a cure [24]. Han et al. compared plication to repeat MUS in the setting of MUS failure and reported a 53% failure rate of plication, compared to 38% failure of repeat MUS [25]. In conclusion, a few small retrospective studies have demonstrated a reasonable success rate of sling plication in the MUS failure population, with plication after RP sling being more successful than TO slings. Furthermore, plication also carries with it an added risk of bladder outlet obstruction. When compared to repeat MUS, plication was not as successful.

Surgical Therapy

The majority of the literature on management of recurrent SUI after previous surgical therapy focuses on the success rates of repeat surgical procedures in patients who received *any* prior surgical therapy for SUI, not specifically MUS, and in many studies includes bulking agents as a surgical option. This finding is likely an attempt to boost the number of patients being evaluated in the studies. Notably, as will be discussed, there are a wide variety of surgical interventions used to manage recurrent SUI after a previous surgical procedure and a common characteristic for all recurrent procedures is a lower success rate when compared to primary procedures for SUI [21••]. Smith et al. demonstrated this in their retrospective review of 637 patients who underwent sling placement for SUI at a single institution and achieved an 81% success rate for primary SUI compared to only 55% success with repeat slings used for recurrent SUI after a previous incontinence procedure ($p < 0.0001$) [26]. As we will discuss, the surgical options for secondary and tertiary management of recurrent SUI include the retropubic "Burch" colposuspension, autologous pubovaginal sling, mid-urethral sling and artificial urinary sphincter (AUS).

Retropubic "Burch" Colposuspension

The retropubic "Burch" colposuspension, as discussed earlier, was historically used to treat SUI prior to the popularization of slings and remains a viable option in the MUS failure population. Specifically, the Burch colposuspension is an effective option for the management of SUI due to ISD, but is not as effective or durable as the PVS [18]. Furthermore, it also addresses the issue of persistent hypermobility [18]. The majority of the studies discussing the effectiveness of this procedure tend to be (late 1990s and early 2000s), likely reflective of the recent popularization of sling use in salvage procedures. There are two small retrospective studies consisting of 13 and 16 patients each who underwent an open or laparoscopic Burch colposuspension after a failed MUS. These studies showed objective cure rates of 77 and 54% at a median follow-up of 1 and 2 years respectively [27, 28]. Moore et al. report a 90% cure rate of a salvage Burch colposuspension in their retrospective review of 17 patients treated with a prior incontinence procedure [29]. In addition, Nikolopoulos et al. report a pooled objective cure rate for colposuspension of 76% in their 2015 review article [21••]. Thus, the Burch colposuspension remains a reasonable option in the failed MUS setting with respectable cure rates reported in the literature. However, the studies tend to be older, to have small numbers, and to be retrospective in nature. Furthermore, the procedure has the benefit of treating SUI due to ISD, similar to the PVS, but unlike the MUS. Drawbacks to the Burch procedure are that it is invasive and its use is dependent on the surgeon's training and familiarity with the procedure.

Salvage Autologous Pubovaginal Sling

Autologous PVS is a well-documented management option in the salvage setting after failed MUS and has been described as a preferred management option for recurrent SUI secondary to ISD or mesh erosion [18]. In their review, Kavanagh et al. highlight a lack of strong evidence for salvage PVS, reporting that most studies are retrospective with a small sample size. They also note a preference for PVS over repeat MUS in patients with severe, recurrent SUI and repeat MUS in those with mild to moderate recurrent SUI, but do suggest, based on expert opinion, that PVS be offered for treatment of isolated, recurrent SUI in patients with more than one failed MUS [6••].

Petrou et al. published a retrospective review of 21 patients who received salvage autologous PVS after a previous failed RP MUS, where 52% of patients remained dry at 74-month follow-up [30•]. Milrose et al. evaluated 66 women with 1 or

more failed MUS who were then treated with an autologous PVS and reported a subjective cure rate of 69.7% at 14.5-month follow-up. Notably, patients with pure SUI were more likely to be cured than those with preoperative mixed urinary incontinence (MUI) (62.5 versus 30%, $p = 0.006$) [31•]. Similarly, Walsh et al. retrospectively examined seven women treated with PVS after failed MUS and had a 71% subjective cure and 86% patient satisfaction rate. However, 80% of patients treated with PVS developed de novo urgency/frequency at 5-year follow-up [32].

In 2016, Parker et al. performed a prospective study of 59 patients to evaluate PVS success in the MUS failure setting and found no difference in objective or subjective cure rates (55.9 versus 62.4%, $p = 0.37$) and (66.1 versus 69%, $p = 0.75$) when compared to patients undergoing placement of an initial PVS for SUI management. However, their cohort of secondary PVS patients after prior MUS did have an increased rate of urinary retention requiring CIC (8.5 versus 3.1%, $p < 0.001$) and re-operation (13.6 versus 3.5%, $p = 0.01$) for persistent incontinence [33•]. Lastly, in their 2015 review, Nikolopolous et al. concluded that PVS for recurrent SUI management has a 79.3% pooled success rate, although this was not specifically in the failed MUS setting [21••]. In conclusion, the literature shows that PVS is a good option for patients after a previous, failed MUS, especially in those who lack urethral hypermobility and thus may have recurrent SUI due to ISD or who may have a history of previous mesh erosion and radiation or desire an alternative to a mesh procedure.

Repeat or "Salvage" MUS

Repeat or "salvage" MUS is another surgical technique for management of refractory SUI with favorable subjective and objective success rates. While not as effective as a first time MUS, repeat MUS for recurrent SUI does come close [3]. Overall, a meta-analysis of prospective cohort studies showed a subjective cure rate following MUS placed for recurrent SUI after any previous incontinence surgery to be 78.5% [3]. Similarly, Jain et al. report a 70–75% subjective cure rate of repeat MUS after a previous, failed MUS in their systematic review [34]. Furthermore, Verbrugge et al. retrospectively reviewed 80 women with a history of MUS failure, who underwent repeat MUS with a mean follow-up of 44.8 months and found an overall subjective cure rate of 61% and subjective improvement rate of 74%, which is remarkable. However, repeat MUS was not without side effects, as the incidence of de novo urgency in this study was significant at 8.2% [35].

The issue of whether or not to remove mesh when replacing a MUS remains a matter of debate and is not well described in the literature. Kavanagh et al., however, advocate for mesh removal if no urethral hypermobility on exam and that is our practice as well [6••]. Furthermore, there have been reports that excision of the prior MUS results in better satisfaction rates than simple release of the previous sling, 84.6 versus 74% respectively, though this was not statistically significant ($p = 0.63$) [35]. It is the practice of these authors to remove prior mesh when replacing a MUS.

In addition, studies have addressed whether TO or RP MUS is preferred in the salvage setting with RP MUS showing a superior subjective cure rate to TO MUS [5, 21••]. Van Baeleen et al. confirmed the superiority of the RP MUS in the salvage setting, attributing its success to its application in the ISD clinical scenario, where the TO MUS does not address ISD. At the mean follow-up of 16 months, physician-determined cure was achieved in 55% of patients, improvement in 15%, and failure in 30%, while the International Consultation on Incontinence Questionnaire at the mean follow-up of 17 months showed a cure rate in 53% of patients, improvement in 5%, and failure in 42% of patients [36]. Lastly, Lee et al.'s retrospective review of 31 patients who underwent repeat MUS for treatment of SUI after MUS failure showed higher cure rates with the RP than TO approach (92.3 versus 62.5%) respectively. The overall cure and improvement rates, irrespective of the MUS approach, were still high (75.9 and 6.9%) respectively [37].

Overall, repeat MUS after failed MUS or other previous incontinence surgery does not seem to be as effective in treating SUI as a first time MUS, but does have reasonable success and symptom improvement rates. Furthermore, repeat MUS is an especially viable option in patients found to have persistent hypermobility of the urethra after their first MUS [3]. Mesh excision is preferred over mesh incision when placing a repeat MUS and the RP approach has better success rates than the TO approach. In addition, as Zimmern et al. suggest, an important concern for patients with SUI after a previous, failed MUS includes hesitation to undergo a repeat sling and/or preference to avoid additional synthetic material, especially in the setting of synthetic mesh erosion. In these cases, a Burch colposuspension, PV sling, and urethral bulking agent may be good alternatives [7•]. Despite all of these considerations, repeat MUS after a previous, failed MUS is an acceptable surgical management option in the correct, willing patient candidate.

Repeat MUS Versus Salvage PVS After MUS Failure

There are two recent studies that compare repeat MUS to PVS in the salvage setting. In a 2016 study by Padmanabhan et al., 152 patients were treated with PVS and 268 with a synthetic MUS in the salvage setting after a prior incontinence procedure and no difference was found in objective cure between PVS and MUS (68.3 versus 70.6%, $p = 0.743$). However, repeat MUS patients had higher subjective cure rates on QoL questionnaires than salvage PVS patients (73.8 versus 55.6%, $p < 0.001$) [38]. Aberger et al. also performed a

retrospective review comparing 153 patients undergoing repeat MUS versus 71 patients getting salvage PVS after a prior, failed sling surgery and found overall subjective and objective cure rates of 61.4 and 66.1% respectively at 29-month follow-up. This difference was not statistically significant [39•].

Other important considerations raised by Aberger et al. in their comparison of repeat MUS and salvage PVS include the issue of sling erosion or mesh extrusion and post-operative complications. In their study, all patients with sling erosion or mesh extrusion had the mesh excised and a PVS preferentially placed over repeat MUS to decrease the chance of repeat mesh exposure and infection. Furthermore, there was no difference in complication rates between the repeat MUS and salvage PVS groups (17.7 versus 16.9%). Post-operative complications described in this salvage setting are similar to those described in the primary setting, with urinary retention (5.8%) requiring intermittent catheterization being the most common and usually resolving in 61% of cases by 1 month post-operatively. De novo urgency was reported in 5.4% of this patient cohort. Other complications include bladder injury, superficial wound infection, blood transfusion, and vaginal extrusion of their MUS [39•].

In conclusion, salvage PVS and repeat MUS have similar objective cure rates with more repeat MUS patients experiencing subjective cure. However, salvage PVS is preferred over repeat MUS in the setting of ISD or mesh erosion and there is no significant difference in complication rates between the two sling groups.

Artificial Urinary Sphincter

Currently, there are no studies that specifically evaluate the effectiveness of AUS in the management of female SUI after a failed mid-urethral sling. However, there some small retrospective reviews that discuss the use of salvage AUS after "previous incontinence procedures." Valeux et al. reviewed conducted a retrospective review of 215 patients with SUI from ISD, 88.8% of whom had prior incontinence procedures. At 6-year follow-up, 79% of patients were satisfied with their surgical outcome and 65% required no pads. However, salvage AUS in this setting was not without complication, having a 7% explantation rate and 15.3% re-do rate at 8.47 years [40]. Similarly, Chung et al. had good success rates in their retrospective review of 29 patients treated with salvage AUS after a previous incontinence surgery, with patients reporting a significant decrease in pad use from 3.6 to 0.2 pads per day and a continence rate of 70% ($p < 0.01$) [41]. In conclusion, salvage AUS, although not specifically evaluated in the setting of failed MUS, is an option with fairly good patient success and satisfaction rates. However, salvage AUS placement is more invasive than many of the other options discussed and carries higher risks of erosion, infection, and device failure. Thus, one must use caution when selecting the appropriate candidate.

Conclusion

The management of recurrent SUI after a previous surgical intervention remains a complex problem with a variety of complex solutions and the key to management is perhaps best described by Bakali et al., who recommend "starting over" with the work-up of these patients with a detailed history and physical exam and appropriate testing to determine the true cause of SUI [5]. The current literature on the management of MUS failure patients, although sparse, does provide some guidance for therapy, but unfortunately does not show a clear benefit of one approach over others. As discussed earlier, the ideal management for these complex patients should be determined using an individualized approach with a detailed discussion of patient symptoms and goals. In our current practice, we prefer to use either bulking agents, RP MUS, or autologous PV sling, depending on patient preference and the clinical scenario to treat the recurrent SUI.

Compliance with Ethical Standards

The research contained in this study did not directly involve human subjects and/or animals and thus no informed consent was necessary.

Conflict of Interest The authors of this manuscript declare that Dr. Padmanabhan serves as a consultant and speaker for Astellas and consultant for Allergan. Dr. Fontenot has no conflict of interest.

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