Peer Review File
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Review Comments

Reviewer A:
It is a narrative review with numerous flaws to be corrected, and therefore cannot be published in this journal.
Firstly, the topic is not new in the field of urology, so the interest of the article is rather limited. In terms of the structure of the manuscript, the Introduction cannot be so long (it occupies 3 full pages), because the reader gets tired of reading the article and has not really started to read the body of the manuscript. The narrative review is too long, with more than 8000 words. The authors should synthesise all the sections of the manuscript, to make them more summarised and easier to read for the reader. Table 1 is of limited interest to the reader, while Table 2, which is the most important part of the text, should include the bibliographical references of the studies to which each technique relates.
Reply: We appreciate this reviewer's comments. We have made efforts to shorten the introduction (see lines 377-428), although we have added to this as well based off other reviewers' suggestions. We have shortened the review overall so that the manuscript is less than 6000 words. We have included bibliographical references for advantages and disadvantages of each technique where appropriate.

Reviewer B:
Nice and comprehensive overview. The authors should include hypogonadism as risk factor of AUS erosion as this is common and therefore a major factor facilitating erosion. The authors should also consider spending less words on tandem cuff placement as this is an obsolete technique.
Reply:
We thank the reviewer for these helpful comments. We have added hypogonadism as a risk factor (see lines 406-407) and have significantly shortened the section describing tandem cuff placement (lines 542-556).

Accordingly, here are the changes in the manuscript:
Lines 406-407: Another risk factor for poor blood supply is hypogonadism, under the premise that androgens contribute to urethral homeostasis and stability (20).

Lines 542-556:
Tandem cuff

Tandem cuff or double cuff placement uses the rationale that one cuff may not completely attain continence, so placement of a second cuff either distal or proximal should theoretically increase resistance enough to minimize SUI in the absence of complete coaptation of either moiety. This technique though does require further dissection that can further compromise vascular supply (27).

Maurer and colleagues performed a prospective trial of salvage tandem cuff placement versus transcorporal, which demonstrated similar continence rates of 88% and 72% (p=0.37) respectively with no significant difference with respect to infection, erosion, or explantation (36). However, studies have shown tandem cuff placement to have increased rates of failure (16) as well as erosion (37), so tandem cuff placement has fallen out of favor. Additionally, tandem cuffs have not been shown to improve leakage (38).

Even though the theoretical rationale for tandem cuff placement is to increase total resistance to flow, clinical and cadaveric studies have not demonstrated efficacy. Several of these have reported worse outcomes necessitating explantation, which obviates the benefits with this approach.

Reviewer C:

This was an excellent narrative review of considerations for incontinence management in the fragile urethra. One thing that was not discussed that would be helpful to include is consideration of using a lower pressure PRB from the outset in those with fragile urethras to prevent erosion.

Overall I found this a highly informative, well-written, thorough, and useful review and recommend publication.

Reply: We thank the reviewer for the helpful suggestion and have included a study that mentions using the 51-60 PRB and delayed activation at 6 weeks. Here are the changes in the manuscript (line 658-663):

Use of the lower pressure Pressure-regulating balloon

There has been suggestion of using a lower pressure PRB (51-60 cm H_2O) in patients who have had pelvic radiation. However, this was described in only one study. To decrease risk of erosion, Singla and Singla have described their use of the lower pressure PRB preemptively in the radiated urethra, coupled with delayed activation at 6 weeks (21). The authors did not specifically describe how their outcomes differed in patients who underwent this technique from those who did not.

Reviewer D:

very thorough review of contemporary data for this complicated topic. i applaud the depth of this paper. if this paper is going to be published, there is paper from journal of

urology 2020 by TURNS group reviewing risk factors and outcomes for their revision AUSs i did not see in your references. i think this should be reviewed and commented on as it is very topical and applicable.

Reply:

We thank the reviewer for the suggestion and have added this paper to our review (see lines 409-410).

Here are the changes in the manuscript (lines 409-410):

Patients with prior pelvic radiation may have a 5 and 10-year revision-free survival rate of 72.6% and 56.4%, respectively (22). Patients who have had prior AUS erosion are also at increased risk for higher rates of subsequent explantation (23-25).

Reviewer E:

The authors have prepared a well written review on the surgical options for patients with fragile urethra and stress incontinence. The authors cover a vast majority of the literature, with a few exceptions

1) Fragile urethra should be better defined to also include other factors that have been studied-- hypogonadism associated with decreased vascularity should be discussed, and also the impact of prior erosion

2) Should mention those studies evaluating placement of AUS cuff around the bulbospongiosus muscle

3) Any evidence to support the role of a Bladder Neck Cuff in the case of a fragile urethra as a salvage options (particularly patients without prostate cancer and without pelvic radiation of course)

4) What is the role for use of 51-60cm H2O PRB in those with SUI and fragile urethra?

5) What is the role of ProACT in the setting of a fragile urethra, any evidence to support use in this setting instead of a re-do AUS

6) Any role for modifying factors associated with "fragile urethra- such as role of hyperbarics in radiated patient prior to re-do AUS?

Reply: We thank the reviewer for these thoughtful comments and suggestions that would help bolster this paper.

1. **Thank you for these helpful additions. We have included hypogonadism (see lines 406-407) and prior erosion (lines 410-412) as risk factors for fragile urethra. Here are the changes:**
    a. Another risk factor for poor blood supply is hypogonadism, under the premise that androgens contribute to urethral homeostasis and stability (20).
    b. Patients who have had prior AUS erosion are also at increased risk for higher rates of subsequent explantation (23-25).

2. **Thank you for this addition. We have reported on studies sparing the bulbospongiosus muscle. Please see paragraph "Bulbospongiosus preservation," lines 665-686. Here are the changes in the manuscript:**

Bulbospongiosus Preservation **(Lines 665-686)**
During standard urethral dissection, the bulbospongiosus muscle is opened midline and retracted laterally as the posterior urethra lies just deep to this structure (11). Given its anatomic relation with the urethra, it has been hypothesized that preserving this muscle by mobilizing it laterally preserves urethral blood flow, minimizing risk of ischemia (49). Roth and colleagues retrospectively analyzed 21 men who underwent muscle-sparing AUS placement that were identified as high-risk due to a history of pelvic radiation or prior AUS erosion. Fifteen patients completed questionnaires over a mean follow up time of 35.8 months with 10 of 15 considering themselves "cured" or "greatly improved," with no erosions reported (49).

A prospective cohort study by Serra and colleagues was performed evaluating muscle-urethral complex AUS placement (50). 82 patients with a history of prostatectomy, 23 of whom underwent salvage radiotherapy were evaluated with a median follow-up period of 46 months. Overall 63 (76.8%) patients reported cure and 76 (92%) patients met criteria for social continence at initial follow-up, though by the end of the study 18 (28%) of the initially cured patients lost continence. Of these eighteen patients, six were found to have inadequate coaptation on cystoscopy presumed due to urethral atrophy, though no patient underwent revision.

These studies have demonstrated good outcomes with regards to continence, and low rate of erosion. However, neither have a comparative arm demonstrating superiority against muscle-dividing techniques, and further studies are needed to determine if there is benefit for the fragile urethra.

3. **This is an excellent question. Bladder neck cuff placement as salvage treatment for a fragile urethra has been described in this study for two patients who were followed after erosion with cuff at bladder neck (Singla and Singla https://www-sciencedirect-com.proxy.fccc.edu/science/article/pii/S0090429514011066). AUS with cuff placement at bladder neck has had a few reports in patients with neurogenic bladder (Rehder P, Stuehmeier J, Jelisejevas LA, Gulacsi A, Horninger W, Pedrini M. World record: Single AMS 800 artificial urinary sphincter functioning uninterrupted for 29 years in male paraplegic patient. Urol Case Rep. 2020 May 6;32:101240. doi: 10.1016/j.eucr.2020.101240. PMID: 32426235; PMCID: PMC7225619., Yates DR, Phé V, Rouprêt M, Vaessen C, Parra J, Mozer P, Chartier-Kastler E. Robot-assisted laparoscopic artificial urinary sphincter insertion in men with neurogenic stress urinary incontinence. BJU Int. 2013 Jun;111(7):1175-9. doi:**

10.1111/bju.12072. Epub 2013 Apr 2. PMID: 23551759., Bersch U, Göcking K, Pannek J. The artificial urinary sphincter in patients with spinal cord lesion: description of a modified technique and clinical results. Eur Urol. 2009 Mar;55(3):687-93. doi: 10.1016/j.eururo.2008.03.046. Epub 2008 Mar 31. PMID: 18394784) but not necessarily in patients with a fragile/high risk urethra.

We do not feel that adding this study describing two patients would contribute greatly to our paper.

4. **This is a thoughtful question. We have included the one study that describes lower pressure PRB 51-60 with delayed activation at 6 weeks (Singla and Singla), see lines 658-663. However, this study only mentions that it was part of their protocol, and does not thoroughly analyze outcomes for their patients who had the lower pressure PRB versus the 61-70.**

   Here are the changes in the manuscript, lines 658-663:

   Use of the lower pressure Pressure-regulating balloon
   There has been suggestion of using a lower pressure PRB (51-60 cm H_2O) in patients who have had pelvic radiation. However, this was described in only one study. To decrease risk of erosion, Singla and Singla have described their use of the lower pressure PRB preemptively in the radiated urethra, coupled with delayed activation at 6 weeks (21). The authors did not specifically describe how their outcomes differed in patients who underwent this technique from those who did not.

5. **Use of ProACT in patients has been described for those who have failed slings but not AUS (Munier P, Nicolas M, Tricard T, Droupy S, Costa P, Saussine C. What if artificial urinary sphincter is not possible? Feasibility and effectiveness of ProACT for patients with persistent stress urinary incontinence after radical prostatectomy treated by sling. Neurourol Urodyn. 2020 Jun;39(5):1417-1422. doi: 10.1002/nau.24355. Epub 2020 Apr 6. PMID: 32249971.).**

   Since this paper focuses primarily on AUS we believe that this should not be included.

6. **Our literature search did not yield any role for hyperbaric therapy in radiated patients prior to re-do AUS.**

Reviewer F:
This is a superb study -- a very well researched and written article. I believe with this extensive effort you are capable of passing judgement on the AMS 800. It has been around for 50 years. The last improvement was 15 years ago and the 3.5cm cuff has disappointed us. It has the worst survival of any device placed in man requiring 50% of patients to undergo a revision in the first 5 years. What if we were able to teach our patients to deactivate nightly? Surely that would help the "fragile" urethra improve survival from revision. Alas, neither the physician or the patient can figure out how to work the pump and this is not possible. Because you are so knowledgeable from your study you have the right to criticize the manufacturer (and there have been 4) to enhance the pump so patients and doctors can more easily activate and deactivate and protect the urethra from pressure 24/7. A knowledgeable article like this coupled with intelligent criticism might help our patients. Your reviewer is so exasperated with the device I talk patients into a mini-jupette even if they don't want a IPP.
There is a typo on reference 21

Reply: We thank the reviewer for these helpful comments. The typographical error in reference 21 has been corrected. Singla and Singla also suggest nocturnal cuff deactivation, and we have added this (see lines 407-409). Here are the changes in the manuscript:
Although some may suggest there are ways to delay urethral atrophy such as nocturnal deactivation of the cuff, the need for revision or further procedures is high (21).