Peer Review File

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Reviewer A:

Thank you for this paper. While the content provides a reasonable narrative review of AUS and high-risk candidates, the content is somewhat disorganised and includes non-relevant aspects of AUS surgery. I would suggest the authors

The authors thank the reviewer for your thoughtful suggestions and points - we have made edits as per your guidance below:

Comment 1. Eliminate subheadings that probably is irrelevant to AUS such as fistula and penile revascularisation surgery. What does this go to do with AUS surgery? If a patient has a fistula- the management is beyond what AUS can do. Similarly, in penile revascularisation surgery - is it a trauma or ED? How is it relevant for AUS surgery?

Reply 1. We eliminated section titled "rectourethral fistula" see page 24-25 lines 561-576. We acknowledge penile revascularization surgery to salvage the lower urinary tract in cases of both radiation and trauma, is a rare procedure. We have seen 2 to date. However, we believe our case we present highlights an example when vascular insufficiency was believed to be the risk factor for erosion, was then diagnosed and finally treated to salvage an AUS with success.

Comment 2. Focus in-depth on what is actually relevant and pertinent to AUS surgery. For example- for radiation patients- what are the strategies to minimise AUS complications such as timing after radiation, surgical techniques (transcorporal etc), and timing of AUS activation.

Reply 2. Thank you – we have cut down on several sections to focus on relevant pathophysiology and surgical techniques:

Removed parts of section prior pelvic radiotherapy lines 163-176

Removed parts of PFUI starting page 10 line 212-229, 237-247

Removed parts of low testosterone section page 17 starting line 379

Removed section of radiation cystitis page page 18 lines 408-417

Removed section titled bladder dysfunction page 19 line 429-439,

Removed section titled rectourethral fistula page 24 from lines 561-576

Removed section of Posterior urethral stenosis page 26 from lines 607-622

Added comment about AUS activation page 36 line 832.

Comment 3. The proposed algorithm is confusing and not well-delineated. For example- is size 12F really that critical.. what about size 14F or presence of longer spongiofibrosis segment??

Reply 3. The authors agree that relative size of stricture is less important and a cut off of 12 Fr is arbitrary. More important factors such as severity of spongiofibrosis and appearance of mucosal health may be more predictive of patient's stricture disease. However those are subjective and endoscopic evaluation may be limiting. Thus, we believe that if combination of stability, lack of clinical symptoms/UTI, and relatively

large diameter of stricture is demonstrated, it is safe to proceed with implantation without urethroplasty.

Comment 4. The authors need to emphasis that in some instances- AUS surgery is not possible or unsafe to be undertaken (such as those who had 2-3 failed revision AUS in the past)
Reply 4. The authors agree that ultimately patient factors such as multiple erosions and prostatic fossa calcifications predict severe disease states and that LUT should be abandoned. This is highlighted in page 25 line 582 “abandonment of the lower urinary tract may need to be considered.” Also added comment line 587 regarding cystectomy and LUT abandonment.

Comment 5. Also it is important to let readers know that size (tightness) of AUS cuff means more likely to have urethral atrophy and/or erosion.
Reply 5. Our section titled “Cuff size and transcorporal placement” page 30 starting line 704 describes that for patients at high risk, conservative sizing is recommended.

Reviewer B:

Comment 1. Summary statement: The authors performed a narrative review of literature on AUS, concentrated upon factors associated with complications including device explanation, revision, infection and erosion.

Type of study:
Scoping or narrative review

Level of evidence:
• Level 3-4 systematic narrative review of case series and heterogenous retrospective cohort studies

Statistical approach: N/A

Strengths: The narrative review is extensive with > 100 references. The authors examine the vast literature on the topic of AUS outcomes and examine the role of multiple important patient factors on outcomes. Some of these factors include: (1) comorbidities including obesity, coronary artery disease, and diabetes, (2) etiology of incontinence, including pelvic fracture urethral injury, post radiation, (3) urethral / bladder pathology, such as radiation necrosis, posterior urethral stenosis, radiation cystitis, and (4) prior surgeries including urethroplasty, previous AUS erosion or explantation.

Weaknesses:
The narrative review is very long and at times somewhat repetitive. It would benefit

potentially from decreasing the scope of the review – such as addressing radiation cystitis as a separate section.
Reply 1. Thank you – we have cut down on several sections to focus on c pathophysiology and surgical techniques:
Removed parts of section prior pelvic radiotherapy lines 163-176
Removed parts of PFUI starting page 10 line 212-229, 237-247
Removed parts of low testosterone section page 17 starting line 379
Removed section of radiation cystitis page page 18 lines 408-417
Removed section titled bladder dysfunction page 19 line 429-439,
Removed section titled rectourethral fistula page 24 from lines 561-576
Removed section of Posterior urethral stenosis page 26 from lines 607-622

Specific comments:
Comment 2. Line 328 deprivation is misspelled
Reply 2. Corrected spelling page 18 line 395

Comment 3. Line 456 – sentence structure erroneous - three was no recurrence of stenosis and 50% were completely dry and 50% required 1-2 pads per day.
Reply 3. Corrected spelling and structure of sentence page 26 line 603.

Comment 4. Line 627 – Tutoplast, I don't agree that you would open onto the rear tip extenders. I have done an AUS several times at IPP and the location of the corporotomies is significantly distal to rear tip extenders, which are beyond the crus of the corporal bodies.
Reply 4. Removed "ideally the rear tip extenders in case of an inflatable device page 33 line 783.

Comment 5. Impact:
Strong – Well performed narrative review that should serve as an excellent resource for surgeons. The authors present several very helpful algorithms for evaluation and treatment. The study is exceptionally well organized and written.
Reply 5. Thank you for your thoughtful comments and corrections. We hope that the removal of several sections will serve to focus our review of the existing techniques and highlight the relevant data and tools surgeons have to treat these highly complex patients.

Reviewer C:

Comment: The authors present a comprehensive analysis of risk factors for AUS failure and provide useful strategies to decrease complications involving algorithms for high-risk patients - these pathways may be extremely useful to standardize care especially for lower volume surgeons and varied settings where complex cases may not be seen as often.
Specifically, the authors note that conformation of urethral stability and optimization of

urethral health as well as careful patient counselling and management of expectations are very important.
This paper would form an excellent addition to the literature to improve outcomes following AUS placement and I congratulate the authors on a very well-written and thoughtful project.
Reply. Thank you for your thoughtful comments. We recognize the heterogeneity that is seen in these high-risk patients and hope this may serve urologists as a guide and algorithm when dealing with multiple risk factors.

Reviewer D:

Dear authors,
i congratulate for this very well written review on a very specific topic of high risk patients.
I only have a few comments on this review:
Thank you for your thoughtful comments and corrections regarding clarity in the methodology.
Comment 1. Please do not refer to tables/figures in the abstract
Reply 1. Removed references page 2 line 43, page 3 line 46

Comment 2. Line 52; please add also bulking agents.
Reply 2. Added on page 4 line 54

Comment 3. Line 79 Pleas remove, this should not be part of the titles?
Reply 3. Removed page 5 line 83

Comment 4. Methods please describe how many reviewers selected the studies, and how agreement on inclusion of studies was performed?
Reply 4. Search strategy was better described on table 1. Added which authors performed screening and review of literature page 5 lines 79, 81.

Comment 5. Methods: For overview purposes, it would be helpful to describe (or table?) which risk factor has been classified to which pathophysiology. E.g. Bulbar compromise: Prior pelvic radiation, prio pelvic frature urethral injury, ….
Reply 5. We describe these in the results section which serve to break the paper into outline format on page 5 lines 95-102

Comment 6. Figure: please add referene (a, b, c) to the picture directly
Reply 6. We added reference to the figures directly as per suggestion page 40 line 877.

Comment 7. How many “experts” have been consultat and furthermore, did you use the delfi method to find agreement on specific topic? Has the agreement procedure of experts depending on a majority voting? If yes, it would be interesting the include the

strengths of rating (percentage of agreements). Please add to the methods
Reply 7. We performed a comprehensive, non-systematic review of all the literature as per search in pubmed. We have edited the methods page 5 line 74 to reflect that as such.

Reviewer E:

Comment 1. I commend the authors on taking on a large topic and reviewing the data well. They offer helpful insight based on clinical expertise where evidence is weak or unavailable. In places the depth of the review and content seems to depart from the stated goal of the piece. Given the length (~8900 words) these departures substantially detract from the readers ability to better understand high risk AUS care. The depth of the review on PFUI, re-vascularization and radiation in particular are out of place and I would recommend significant trimming of each as detailed below. Would recommend aiming for <4000 words.
Reply 1. Thank you for your thoughtful comments and corrections. We hope that the removal of several sections will serve to focus our review of the understanding of the pathophysiology, role of existing published techniques, and highlight the relevant data and tools surgeons have to treat these highly complex patients.

Comment 2. Introduction:
Good lead-in for the topic. Add in vascular injury/pelvic trauma, testosterone, etc if you want to include later. Based on the tone and focus of the paper these topics don't seem to fit in the manuscript.
Reply 2. Added comment about how injury/radiation have similar pathophysiology, ultimately resulting in vascular compromise. (similar to how testosterone decreases density of vessels later described). Page 4 line 63-64.

Comment 3. Methods:
-Identify screeners
Reply 3. Added screeners on page 5 line 79, 81.

Comment 4. Results:
Include total number of articles found by search and included/excluded.
Reply 4. Added number on page 5 lines 87-89

Comment 5. Can you expand on why pelvic fracture related injury expertise is relevant?
Reply 5. Added comment on page 5 line 90. Sentence reads: "our knowledge of the patholophsyiology of PFUI can be applied to inform care with SUI after prostate surgery and/or radiation, another form of injury to the genitourinary organs"

Comment 6. No prior discussion of blood flow/vascular compromise in introduction. This whole discussion seems out of place
Reply 6. Added comment regarding vascular compromise in introduction on page 4 line 63-64.

Comment 7. Discussion
For the discussion I would recommend organizing by what the reader is going to be most interested in. Assuming the audience is likely reconstructive or general urologists (including trainees) who treat men with SUI I would suggest shortening the paragraphs on risk factors to just data on how these interact with AUS placement. This will allow for more space on the surgical approaches which I think will be a of greater interest to the reader.
Reply 7. Thank you for the very thoughtful thoughts on the structure of our paper, especially on exclusion of sections and data on less relevant pathophysiology. We hope our edits have made this paper more concise and focused so that urologists can hone in on the complexities of high-risk patients.

Comment 8. Risk Factors/Bulbar urethra
a.Pelvic Radiation
Don't see a need for a review of radiation mechanism. Not sure this promotes the goal of improving provider understanding of options for management of high risk SUI
Can authors comment on why there might be a decline in the negative role of radiation after first implant? Is this a selection bias that only the healthier patients are getting a third implant?
Reply 8. Removed parts of section on prior pelvic radiotherapy lines 163-176 as per guidance.
The authors postulate that for the first erosion, patient factors play a larger role be it radiation or advanced age or diabetes. However, after first erosion, the more influential factor is the prior erosion leading to subsequent erosions. And furthermore the lack of difference in time to erosion, that was initially seen on first erosion compared to subsequent erosions. We hint at this however do not elaborate as this is a hypothesis from one study (Fuller et al). This is mentioned on page 10 line 199-209. We added "such as prior erosion" to help clarify this point on line 207.

Comment 9. b.Pelvic fracture
Need to add this to the introduction if there is a desire to include. This seems disjointed from the topic overall as the other mechanisms for SUI were isolated to post-prostate intervention
Reply 9. Added to introduction page 4 line 63-66

Comment 10. Inclusion of steps to address blood supply during PFUI repair seem out of place
Reply 10. Removed section on discussion of techniques to preserve blood supply page 12 lines 254-262

Comment 11. Recommend removal of majority of this section and limiting discussion to the final 2 paragraphs which discusses AUS approach in PDUI patients.
Reply 11. Trimmed section starting from page 10 lines 216-220, 227-229, 231-233,

lines 242-251

Comment 12. c. Urethroplasty
-Good review. Like the discussion on the possibility of blood supply role in transecting v nontransecting
d. Prior Cuff erosion
-Lengthy discussion but major part of manuscript. I would recommend moving this to the first subsection given many readers will want to jump to this section.
Reply 12. Moved to first subsection page 6 line 111

Comment 13. e. Testosterone
-Too long. Data from Hofer et al can be more succinctly summarized. Should be single short paragraph.
Reply 13. Summarized the data more concisely. Removed from page 17 lines 383-385, 387-388, 390-391, 392-393.

Comment 14. Bladder pathology
a. Radiation cystitis
- Remove the introductory remarks on radiation
Reply 14. Removed remarks on radiation page 18 lines 412-417, 419-421, 434-436, 438-443
We also restructured this section to
"Radiation induced bladder pathology"
"Pelvic fracture related bladder pathology"
"Need for lower urinary tract instrumentation (bladder cancer, CIC, hemorrhagic cystitis)"

Comment 15. The discussion of bladder cancer is also important. Would break out as its own subsection for that paragraph
Reply 15. Added this to the section titled "Need for lower urinary tract instrumentation (bladder cancer, CIC, hemorrhagic cystitis)" on page 21 line 483

Comment 16. b. Bladder dysfunction
-Shorten discussion on radiation and bladder dysfunction (can remove whole first paragraph)
Reply 16. Removed remarks on radiation page 18 lines 412-417, 419-421, 434-436, 438-443

Comment 17. Paragraph beginning line 398 doesn't fit
Reply 17. Broke this out into its own small subsection "Pelvic fracture related bladder pathology" page 20 line 463

Comment 18. CIC discussion is important. Make it it's own paragraph/section
Reply 18. Added this to new section "Need for lower urinary tract instrumentation

(bladder cancer, CIC, hemorrhagic cystitis)" starting page 21 line 475

Comment 19. LUT complications
a. Fistulae
-Again the focus is pulled away from a discussion of SUI in this population and there is small review of RUF. Could you instead comment on AUS placement in the setting of prior RUF repair including considerations where gracilis was previously used.
Reply 19. Removed entire section on fistula page 22 line 504
Added portion regarding gracilis interposition on page 31 line 731

Comment 20. b. Calcifications
-This is a great paragraph. Keeps focus on SUI and good figures. Would appreciate comment on cystectomy v not at time of diversion in these patients.
Reply 20. Added comment regarding cystectomy on page 26 lines 591-594: "If the patient elects for non-continent urinary diversion, the authors recommend safe resection of bladder tissue and mucosa. In hostile pelvises, as seen in patients with prior radiation and surgery, a partial cystectomy may be performed with fulguration of any remaining bladder mucosa."

Comment 21. c. PUS/VUAS:
-Can skip paragraph starting line 459. Again focus should narrow on SUI management not a review of posterior urethral stenosis management.
Reply 21. Removed paragraph page 26 line 611

Comment 22. Line 479 offers great insights. Expand on cost and what this space-saver approach offers.
Reply 22. Expanded on the benefits of this approach on page 27 lines 633-637

Comment 23. d. Anterior urethral stricture
-Best section of the manuscript. Consider moving this up to highlight for reader.
Reply 23. Moved up to be the first subsection on page 22 line 504

Comment 24. B. Surgical considerations
The discussion of prior PFUI and/or radiation can likely be limited to one paragraph here. This section should be the main focus of the paper and discussion.
Reply 23. We elected to summarize this more succinctly and removed less relevat sections on pathophysiology as per above on section "bladder dysfunction"

Comment 25. Can you expand on timing of follow up? How frequent do you do cystoscopy.
Reply 25. We added statement regarding delayed AUS activation on page 36 line 837: "Surgeons may consider delay in device activation for up to 8 weeks or longer after implantation in high-risk patients."
While authors do not regularly perform cystourethroscopy in high-risk patients, we do

evaluate the mucosa, ensure patency of repair and exclude gross erosion at about 3-6 months. The authors rely more on strict patient instruction to seek urologic care when signs of device failure/erosion arise.

Reviewer F:

Comment 1. This is a thorough review article, addressing a difficult patient population. A few minor issues should, in my opinion, be clarified further:
Reply 1. The authors would like to thank the reviewer for the thoughtful review and points of clarification. We hope the edits made clear our points in a succinct manner.

Comment 2. Lines 210-212: Do AUS with bladder neck cuff tend to show better device longevity in these patients? Please explain more clearly.
Reply 2. Added comment for clarification: page 13 line 279-282: "Few studies have compared bulbar urethral AUS cuff placement to bladder neck AUS cuff placement, though Khene et al saw a trend towards longer explant-free survival in patients with bladder neck AUS with median explant-free survival of 18.5 years in bulbar urethral AUS cuffs and 24.5 years in bladder neck cuffs."

Comment 3. Lines 366-368: How do these patients benefit from device uncoupling? And why would they benefit more from this invasive surgical procedure than from simply deactivating the device? Please clarify.
Reply 3. Added paragraph clarifying when to simply deactivate vs uncouple for 1 procedure vs leave uncoupled. This starts on page 21 line 488-501.

Comment 4. Line 441: Calcifications (plural).
Reply 4. Corrected page 25 line 589

Comment 5. Lines 452-453: This is difficult to understand. Do you mean to say that all of these 8 patients received a space-saver, which then had to be removed due to infection in 3 patients? Or did only 5 patients receive a space-saver in the first place? And what type of lower urinary tract reconstruction did these 8 patients receive after cystoprostatectomy? A neobladder? Please explain more clearly.
Reply 5. Added several words for clarification: "with orthotopic neobladder page 26 line 602.
Edited: "While 5 of 8 patients underwent placement…" page 26 line 604

Comment 6. Line 456: "There" instead of "three".
Reply 6. Corrected page 26 line 607

Comment 7. Line 676: I think it should read "to both ensure patency of the repair and EXCLUDE gross erosion".
Reply 7. Corrected to add "exclude" on page 36 line 842

Comment 8. Line 679: Missing an "of" ("after a period OF deactivation").
Reply 8. Added word on page 36 line 851