

Peer Review File

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Review Comments

Reviewer A

I had the opportunity to review "Penile Fibrosis - Still Scarring Urologists today: A Review Article" For TAU. Please see my comments below. The biggest take home is that the review article needs some visual aids - figures and/or tables.

Title:

-Great!

Abstract:

-No changes recommended - nice overview of the article

Introduction:

-Paragraph 1 - can you expand on the implications of reduced cell number and myofibroblast accumulation? What does this mean from a mechanism standpoint and how does it result in fibrosis (or vice versa)?

A: Added

“In addition, there is a reduction in functional smooth muscle cell numbers and an accumulation of myofibroblasts leading to loss of corpora cavernosa sinusoid architecture, disorganized extracellular matrix, excessive collagen deposition, and scar contraction. Overall, this pathophysiology results in penile length loss and/or curvature (2).”

Methods:

-This is more of a "narrative review" - might want to comment on that and acknowledge that it is not an official review article following associated guidelines

A: Added

We conducted a narrative review searching PubMed for publications with key words: “penile fibrosis”, “scarred corporas”, and “fibrosed corporas”.

Preoperative Eval and Considerations:

-Rather than stating that patients should be referred to academic institutions, I think just stating that patients should be referred to high volume surgeons with expertise in managing these complex patients. I'd argue that there are many academic institutions who do not have this expertise.

A: Removed academic institution and replaced with high volume..

However, in our experience, cases of severe fibrosis are frequently referred to high-volume practices that specialize in prosthetic surgery to address this difficult scenario.

Patient satisfaction

-In the first paragraph of this section, the authors immediately jump into discussion about post-infectious fibrosis. I'd suggest moving this later in the section after the second paragraph and expanding more on infection and other etiologies for fibrosis as it pertains to satisfaction.

- Moved to second paragraph of section.

- infection/priapism/other causes fibrosis are alluded to later in manuscript.

-Second paragraph - Please expand upon the statement "if a full inflatable prosthesis is desired, more than one surgical procedure may be required...."

- amended sentence to say "If a standard-dimension 3-piece inflatable prosthesis is desired, more than one surgical procedure may be required to reach a satisfactory outcome, using the smaller devices as a temporary spacer."

- See "Downsizing and upsizing cylinders", starting on line 445 for more discussion.

Cavernotomes / Types of penile prosthesis

-Please include photos / figures - this will greatly enhance these sections

- Done see Table 1

-May also consider a table as adjunct or alternative

- Done see Table 1

Techniques with scar incision

-Same thing - it would be great if there were some visual aids here

- Do you want to put intraop photos or have me search some?

Conclusions

-Nice!

Reviewer B

very comprehensive review. Nice work

-penile ultrasonography: please comment on value of elastography

- Added "Two-dimensional shear wave elastography (2D-SWE) is a newer technique whereby soundwaves on US exam can cause shear waves that transversely propagate through tissue that can be measured to estimate tissue stiffness. Stiffer tissue on elastography is strongly correlated to fibroblast activity and collagen deposition.¹ Richards et al have shown in humans that 2D-SWE imaging finds tissue involved in penile curvature that has is firmer by elastography measurement than normal tissue despite no findings on standard US or palpation.² Other authors have shown an increase in elastography to be correlated with ED, Peyronie's disease, age^{3,4}. Finally,

penile shear wave elastography may be used in future studies examining protocols to reduce fibrosis preoperatively by estimating the relative amount of smooth muscle cells and elastic fibers in the penis before and after interventions.

-please involve discussion on penile length measurement pre-op”

-intra operative tools: add otisurthrotome and "TUR" loop resection, see line 384

- If a dedicated cavernotome is unavailable, the Otis Urethrotome has also been described however we would advocate that complex cases be done at high volume centers who have dedicated intraoperative equipment suitable for the task,⁶

- added (or, alternatively a transurethral resection loop) to line 422.

-line 346 transverse or longitudinal penoscrotal incision?

- added “midline longitudinal” to line 369

-other techniques (line 440): comment on "tunneling technique"

-tunnelling techniques are described 419-428

-penile implant infection: mention immediate salvage with inflatable device (Jang et al. IJIR, 2022)

-added short discussion on salvage line 506: “Dr. Mulcahy in 1996 described a salvage technique involving removal and immediate replacement with a malleable penile prosthesis (MPP) at time of removal and infection wash-out.⁷ Jiang et al conducted a multi-institutional retrospective cohort study on immediate IPP after infection and describe a high success rate after a full Mucahy washout with recurrent infection occurring in 3 of 19 (15%) cases and 1 reservoir hernia. They did not find any prognostic factors in predicting postop recurrent infection but do demonstrate similar infection rates as replacement with MPP.⁸”

give data on" the more revisions, the higher the infection rates"

- line 130 “Montgomery et al have reported that risk of penile prosthesis infection increases with each subsequent infection: 1st revision case (6.8%; 3/44), 2nd (18.2%; 4/22), 3rd (33.3%; 4/12), 4th (50%; 4/8), and 5th (100%; 2/2)”

Reviewer C

The authors have submitted an excellent review of penile fibrosis. The manuscript is organized well and flows logically. The manuscript would benefit from careful correction of spelling, grammar, and typographical errors.

Title: Today should be capitalized. Also is the second listing after the title the running head or an alternate version of the title?

- updated title to Penile Fibrosis - Still Scarring Urologists Today: A Narrative Review

Abstract: The abstract could be rephrased to some degree. A few of the sentences are not entirely clear.

- no other reviewers had comments. Please indicate sentences are not entirely clear and we will improve the abstract.

Introduction: Please make sure to add corporate headquarters information for all companies, devices, tools, grafts, and other appropriate items listed throughout the paper.

- Done

Methods: Please add to this section a little. We are not asking for a PRISMA-level review, but it would be helpful to flesh out your methodology.

- indicated it is a narrative review and provided keywords and database searched.

Preoperative Evaluation and Considerations: Is the preoperative ultrasound performed with intracavernosal injection?

- Typically without given not expecting erection/success of injection..

Intraoperative Tools: It would be nice to identify the creators of other tools since Dr. Mooreville was also highlighted. It would be more appropriate to refer to him as Dr. Michael Mooreville.

- done

Surgical Techniques: This section is very thorough.

Special Considerations: This section is also very thorough.

Conclusions: No concerns

References: The reference formatting is highly variable.

Conclusion

- Need to fix

Reviewer D

There are some modifications that need to be done in the manuscript

In line 108: "corporas" (corpora)

In line 128: "International"(missing) Index of Erectile Function (IIEF)

In line 200: "ration" should be "ratio"

In line 202: "reduce" should be "increase"

In line 256: "Furlough" should be "Furlow"

In line 362: "SRPP" abbreviation for "Semi-rigid penile prosthesis"

And the whole sentence can be modified into "In their series, 7 patients had semi-rigid penile prosthesis and 5 patients had IPP successfully placed.

In line 478: "the of" should be "of the"

- Fixed

Also, there is a recent technique prescribed recently that has not been mentioned in the article called the unfolding technique in which the fibrous tissue core is used to expand the tunica albuginea to accommodate a large sized penile prosthesis with minimal complications.

The “Unfolding” Technique for Penile Prosthesis Implantation in Post-priapism
Corporeal Fibrosis

<https://doi.org/10.1093/jsxmed/qdad060.385>

<https://www1.statusplus.net/misc/videos/issm/issm-smsna2022/search/video/?url=https://vimeo.com/756749235&redirect=pm>

- Added “Finally, Dr. Rassoul described an “unfolding” technique in 15 cases post-priapism. In this technique, the urethra is dissected away from the corpora, fibrosed corpora are divided medially and, the septum filleted open and unfolded along the length of the shaft. The corpora are then dilated proximally and distally using cavernotomes. A MPP placed within the larger combined space and corpora are sutured together in midline. They describe successful surgery in 13 of 15 patients with 2 reports of infection but no crossover or urethral injury.⁸ However, this technique requires both a circumcising incision, degloving and delivery of the penis through a midline longitudinal perineal incision. It also requires extensive dissection/mobilization of the penile urethra. Therefore, we advise caution in adopting this technique, as retrograde and antegrade flow to the glans may be disrupted causing glans necrosis.⁹”

Reviewer E

In the methods section, in addition to the search terms used, it would be useful to communicate the number of initial articles found and those that were finally included after being discarded. Due to the difference in quality, it would be positive to know whether single clinical cases were included, as well as case series or other types of superior studies.

- Changed methods section to read ” We conducted a narrative review searching PubMed for publications with search strategy: "penile fibrosis" OR "scarred corporas" OR "fibrosed corporas". This search returned a total of 137 articles. Of the total articles returned, 34 were review articles, 2 systematic reviews, 3 randomized controlled trials (involving alprostadil for ED), 10 non-randomized clinical trials, and the remaining 88 articles were retrospective case reports/case series discussing prevention and/or management techniques. This review was intended to provide expert commentary on the topic and not intended to be a systematic review. We prioritized articles in which the surgical techniques for placement of a penile prosthesis in a fibrosed corpora were described, especially those that also presented their outcomes and results.”

I would add some reference to the paragraph: Preoperative Evaluation and Considerations (line 112-118).

- added reference citation “Penile Prosthesis Complications: Planning, Prevention, and Decision Making Scherzer N, Dick B, Hellstrom W *Sexual Medicine Reviews* (2019) 7(2) 349-359”

Reviewer F

An extensively detailed and referenced review article that has successfully encompassed the scope of penile fibrosis in the light of penile implant surgery. The article is well written and would be a valuable addition to TAU.

Please add in the methods section how many articles were reviewed for this review article, and how many were dealing with surgical techniques to manage and/or prevent corporal scarring.

- - Changed methods section to read ” We conducted a narrative review searching PubMed for publications with search strategy: "penile fibrosis" OR "scarred corporas" OR "fibrosed corporas". This search returned a total of 137 articles. Of the total articles returned, 34 were review articles, 2 systematic reviews, 3 randomized controlled trials (involving alprostadil for ED), 10 non-randomized clinical trials, and the remaining 88 articles were retrospective case reports/case series discussing prevention and/or management techniques. This review was intended to provide expert commentary on the topic and not intended to be a systematic review. We prioritized articles in which the surgical techniques for placement of a penile prosthesis in a fibrosed corpora were described, especially those that also presented their outcomes and results.”

Reviewer G

Excellent review

There are a number of spelling and grammatical errors.

line 127 that should be who

line 126 their should be his - also in numerous other locations

line 171 corporas should be corpora - Corpus -singular corpora - plural

line 171 - Brooks should be Brooks dilators

line 200 - ration should be ratio

plus other errors

- Fixed

What is the latest status of the Carrion cast. Is it used and widely recommended? The manuscript is unclear about this.

- For those patients in which salvage implantation was not a possibility, several options have been described to prevent the imminent fibrosis thus allowing placement of a new implant with less complication. At the University of South Florida Dr. Carrion and his team (62) presented the use of an antibiotic impregnated, high purity calcium sulfate component as a temporary spacer at the time of removal of an infected penile prosthesis. The “Carrion cast” typically takes 4-6 weeks to dissolve. As it dissolves, it provides constant delivery of antibiotics to the local tissue. In their

preliminary series (n=2), they noted that when the implant is placed within 6 weeks, dilation and implantation was uneventful and no special techniques were required. Due to social reasons the one patient underwent re-implantation at 16 weeks and significant fibrosis was encountered (63). This technique continues to be refined and is not widely used.

Are there good studies that document the effectiveness of the medications mentioned to reduce fibrosis? or are they recommended because they might work based on their mechanism, as is the case with many of the medications employed to reduce Peyronie's plaque development?

- Recommended based on theoretical mechanism as described. No strong evidence.

Reviewer H

This is an excellent review of a difficult scenario encountered by prosthetic urologists. Only the following minor issues requiring revision/correction are identified:

line 117-spelling

line 239-240-angled toward the urethra? Is this correct?

line 470-476-description of the Carrion cast procedure should be enhanced-please describe the technique in detail. Also, 475-6, the issue with "social reasons..." needs to be expounded upon, as this is unclear.

- I do not know what happened in this case. Please address.