Peer Review File

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Review Comments

Reviewer A

The authors' dedication to collecting and meticulously tabulating the data is commendable, showcasing their commitment to producing a high-quality study. However, while their efforts in data collection are praiseworthy, it is crucial to recognize the potential for a more comprehensive and insightful analysis of the complications associated with these procedures.

To guide the readers effectively, the authors should consider presenting the findings in an unbiased format, allowing for a more objective understanding of the risks and benefits involved. Such an approach could significantly enhance the study's impact on the existing literature, serving as a reliable reference for both experienced surgeons and those seeking to enter this specialized field.

Comment 1: However, while their efforts in data collection are praiseworthy, it is crucial to recognize the potential for a more comprehensive and insightful analysis of the complications associated with these procedures. To guide the readers effectively, the authors should consider presenting the findings in an unbiased format, allowing for a more objective understanding of the risks and benefits involved.

Reply 1: We appreciate the feedback regarding the manuscript, a great deal of effort was placed into tabulating the data and incorporating all the most recent publications on this topic. All of the surgical approaches outlined have their corresponding manuscripts, and the reported data in the text of that paragraph, for each approach the reported complications are listed with the percentage of that cohort. The majority of these procedures are relatively new without long-term data and for all of them we discuss how "The feasibility and safety of these approaches in all settings cannot be concluded from this article, as it summarizes numerous prior reports, many of which were not randomized with appropriately selected controls, nor prospective." (Lines 520-523)

While information on global risks of penile prosthesis placement in general could be added, the focus is more on the complication profiles that have been reported in those undergoing concurrent lengthening procedures which is included. Anecdotal information on some surgeon experience is included, to discuss minimization of complications, as we do with the TEP procedure discussing our methods of reducing distal ischemia risk, reducing hematoma risk, and how we optimize cylinder sizing. As discussed in the limitations, we do include some of "the senior author's experience, however, without statistical data supporting clinical outcomes and complications," too much commentary can weaken the overall review with bias.

Reviewer B

This is a phenomenal article. It is comprehensive, current, sufficiently explanatory, and well written. My only concern is that the introduction is a tad long, but otherwise I am thoroughly impressed and I commend the authors for their strong work. Please also revise the text once more for minor grammatical errors. Job well done, thanks very much for your exceptional efforts in creating this definitive review.

Comment 1: My only concern is that the introduction is a tad long, but otherwise I am thoroughly impressed and I commend the authors for their strong work. Please also revise the text once more for minor grammatical errors

Reply 1: We appreciate the time that was taken to review the manuscript and the very positive feedback.

We reduced the length of the introduction removing some details that were extraneous to the specific context of this review, the word count of the introduction was reduced from 741 to 613 words. The entire text was reviewed, and numerous minor grammatical errors were corrected, and long, run-on sentences were modified to smaller sentences and re-arranged.

Reviewer C

Images 4A & 4B are placed together in one file. 4B has an image showing horizontal cuts on the tunica albuginea. In this image, there are only horizontal cuts placed in parallel, unstaggered positions at great distances from each other. Based on the mathematical formula, the expansion ratio is very low. Please note that this image should be replaced by a true image of the Egydio TEP strategy showing multiple, small, staggered cuts placed close together. Also, please use the MS Word Review-View-Markup tool to see the substantial corrections made throughout the text of the article.

Comment 1: Images 4A & 4B are placed together in one file. 4B has an image showing horizontal cuts on the tunica albuginea. In this image, there are only horizontal cuts placed in parallel, unstaggered positions at great distances from each other. Based on the mathematical formula, the expansion ratio is very low. Please note that this image should be replaced by a true image of the Egydio TEP strategy showing multiple, small, staggered cuts placed close together. Also, please use the MS Word Review-View-Markup tool to see the substantial corrections made throughout the text of the article.

Reply 1: We have changed the requested images and have utilized new photos. The new Figures are now 6A and 6B based on the recommended revisions within the text and re-ordering of the paper.

Reviewer D

The authors are to be commended for this an excellent review of new techniques to maximize penile length during penile prosthesis surgery. There is little to add except that a short discussion on types of penile prosthesis and effect on penile length may be warranted.

Comment 1: There is little to add except that a short discussion on types of penile prosthesis and effect on penile length may be warranted.

Reply 1: We appreciate the time that was taken to review the manuscript and the overall positive feedback.

We did add a discussion on types of penile prosthesis and effect on penile length at the end of the discussion. The addition to the text reads as “Additionally, device selection is an important component of PP surgery. Numerous devices exist, but the two traditional manufacturers for penile implant in the USA are Coloplast and Boston Scientific [58]. From these companies, devices include the Titan (Coloplast, Minneapolis, MN), Genesis Malleable (Coloplast, Minneapolis, MN), AMS 700 LGX (Boston Scientific, Marlborough, MA), AMS 700 CX (Boston Scientific, Marlborough, MA), AMS 700 CXR (Boston Scientific, Marlborough, MA), Tactra (Boston Scientific, Marlborough, MA). Also, a 2-piece IPP exists the AMS Ambicor (Boston Scientific, Marlborough, MA). While the nuances of each device are out of the scope of this paper, and all devices, can be used during concurrent PLP, 1 device emphasizes length expansion in those without fibrosis or scarring, the AMS 700 LGX (Boston Scientific, Marlborough, MA). In a prospective study of 45 patients, those who underwent AMS 700 LGX (Boston Scientific, Marlborough, MA) implantation had a mean 10% increase (1.3 +/- 0.4 cm) from baseline to 12 months, and an 80% satisfaction rate with penile length without concomitant PLP’s [59]. However, another prior, single armed, prospective, two-center study, this device was able to maintain stretched penile length in only 23.1% of patients. They suggest that implantation of the AMS 700 LGX (Boston Scientific, Marlborough, MA) cylinders alone are not sufficient for increasing SPL but acknowledge that this was prior to their post-operative inflation protocol being implemented that may have improved outcomes [60]. More recently a newer company Rigicon (Ronkonkoma, NY) is offering an IPP that also promotes length and girth expansion, the Infla10 AX. Initial studies with all of their implants have shown freedom from revision comparable to the existing devices, however they are still in the process of obtaining Food and Drug Administration (FDA) clearance in the US [58, 61]. The Rigicon implants (Ronkonkoma, NY) are already available in many countries outside the US, however, at this point, initial published studies report on the first 545 patients implanted with all Rigicon Infla10 devices (34.7% of which are Infla 10 AX, and report similar safety data for mechanical failure, device infection, but do not report on real world impact on penile length preservation [61]. The discussion of which PP should be utilized is another of the many nuances involved in these operations, unfortunately, most manuscripts at this time do not publish their specific device utilization, so direct comparisons is difficult to perform.” (Lines 477-505)

While the specific nuances of each device could be a review paper in itself, we hope this adds the information you were looking for.

Reviewer E

The authors should be congratulated for addressing an interesting topic. However, a lot of points warrant mentions:

Comment 1: In the whole manuscript, an extensive English revision is required. Many sentences are too long and difficult to read.

Reply 1: Throughout the text of the manuscript, we have revised long sentences and broken thoughts up into multiple smaller sentences. Additionally, based on the line numbers submitted in the following comments, it appears the reviewed manuscript was not the final draft that was submitted to TAU for review. We did submit an initial manuscript with those line numbers; however, a revision was requested that had extensive changes, but we will outline the additional changes requested.

Comment 2: In the "Introduction" section, line 74, is it not clear which studies have been considered, is on intervention on Peyronie's disease (PD) or on penile prostheses (the main topic is hidden in the introduction section, which should be better exposed).

Reply 2: The review paper is focused on concurrent penile lengthening procedures in the setting of penile prosthesis placement. This is discussed in the methodology, the pathophysiology by which the patient got to the penile prosthesis may be different, but the ultimate details and the manuscripts reviewed are outlining the concurrent penile lengthening in the setting of prosthetic placement.

Comment 3: In the "Introduction" section, the authors are invited to clarify the aim of the current study and to better expose the rationale behind the study.

Reply 3: We have clarified the current aims of the study better at the end of the introduction. The text now reads "Regardless of the pathophysiology leading to the need for PP, we aim to review and provide an update on the expanding literature regarding techniques to preserve and enhance penile length with PLP during PP. As a whole, the quality of studies published in the literature over the last decade remains low. Scientific evidence regarding efficacy and safety of intervention is lacking. The majority of scientific evidence is based on studies with poor internal validity (observational designs, non-standardized methodologies, heterogeneous populations) and single surgeon experiences. Additionally, most reviews analyze changes in penile dimensions inconsistently, underscoring the lack of consensus regarding safety and efficacy outcomes as well as patient satisfaction, all of which are inconsistently reported [22]." (Lines 96-104)

Further clarifications are provided throughout the methods section as well.

Comment 4: In the "Results" section, the authors are invited to declare firstly the number of selected studies, then the numerosity of studies according to the main topic.

Reply 4: This has been added to the start of the Results section: "Many different surgical techniques have been developed over the last decade. The initial PubMed search returned 152 articles, 29 were excluded for duplication. Abstracts and titles were read for 123 remaining papers. The majority of these articles, were review papers without original data or patient reported outcomes. Additionally, many articles were not specific to penile prosthesis surgery. A total of 18 articles were ultimately included the pre-operative, post-operative and PLP comparison of study results and parameters are summarized in Table 1." (Lines 138-143)

Comment 5: In the "Methods" section, it is totally not understandable how the systematic review has been performed. This section should be written again by specifying the period of study selection, keywords, who has selected studies, inclusion and exclusion criteria, if one or more authors discussed studies to be included, and so on…

Reply 5: We have re-written much of this section to include the recommended details. The context now reads “An extensive, systematic literature review was performed using PubMed over the past 10 years. Search timeline included all results from March 2013 to March 2023. Only studies published in English were included in this systematic review. Keywords used “penile prosthesis” with “penile lengthening”, “penile enhancement”, and “penile restoration”. The search was intentionally broad to allow for wide-review of peer-reviewed papers. At completion of reading prior study, we manually reviewed references of eligible studies to ensure additional publications were not excluded. All authors reviewed and discussed studies to be included. To meet inclusion, all articles had to have subjective and/or objective penile length outcomes. These were then reviewed, and we include only those procedures that are designed to lengthen the penile shaft and not just give the perception of length gain. Additional studies with subject matter important for historical referencing of PLP in this manuscript were included, even if original publication was before 2013. Pre-operative, post-operative and PLP comparison of study results and parameters are summarized in Table 1. A Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow diagram of the study selection process is presented in Figure 1[23].” (Lines 119-133)

Comment 6: The authors are invited to produce a PRISMA flow diagram as part of the results of the SR.

Reply 6: We have added a PRISMA flow diagram, this is our new Figure 1.

Comment 7: Did the authors analyse the risk of bias in included studies?

Reply 7: We did attempt to minimize bias in included studies by looking into numerous journals, literature databases, as well as abstracts with unpublished manuscripts as it is a constantly evolving field. We systematically collected and synthesized the data on all available articles. This specific topic, as we acknowledge at the very beginning, is wrought with poor scientific evidence, poor internal validity with non-standardized methodologies and is largely single surgeon experiences. Given this, it is inherently at higher risk for bias due to higher heterogeneity.

We added the following to our limitations: “Additionally, many of the studies referenced are very small clinical outcomes series, therefore study-level or outcome-level statistical analysis between surgical approaches is not feasible, also this affected the ability to assess for risk of bias, which can be a limitation in systematic reviews [61].” (Lines 515-519)

Comment 8: In the whole “Results” section, the authors should report the results of published literature according to the p-value. It is really difficult to follow this section with only numbers and not statical significance.

Reply 8: While I agree it would be nice to include p-values and statistical significance, almost none of these papers report this information. Those that did, we included. This is already mentioned in the limitations “Statistical analysis in this review was not performed given the fact that several studies only

reported subjective penile length outcomes." The vast majority of these papers are reporting subjective outcomes, not clinical significance in a randomized fashion one approach versus a different so numerical outcomes is all we have for comparison.

Comment 9: In the "Results" section, in the "Pre-operative and Post-operative Protocols" subsection, the authors reported previous studies on pre- and post-operative outcomes according to the use of VED or PTT in patients with PD. An important point that should be reported is the mean curvature degrees of analysed patients and plaque characteristics, considering their influence on post-operative outcomes.

Reply 9: These are important parameters, when included in the published manuscript we added in mean curvature analysis as well as plaque description. However, these were inconsistently reported, so were not included for all of the studies on VED/PTT. We did update all studies including p-values for the measurements as requested in Comment 8.

Comment 10: In the "Results" section, lines 241-253, penile lengthening is not mentioned in these reports. I suggest to eliminate them.

Reply 10: We eliminated the text and reference to the initial study that reported on the technique, but did not provide any penile length parameters.

Comment 11: In the "Results" section, line 285, the authors reported "recurrence of haft deformity", without reporting any deformity before. I suggest to clarify.

Reply 11: This comment was removed. While this is a statement from their manuscript, on additional review, they do not specifically describe the deformities for each patient. They only describe patterns of curvature but do not specify individual parameters nor what they quantified as a recurrence.

Comment 12: In the "Results" section, "Modified sliding technique (MoST)" subsection, results are reported without logical consequence. I can't understand which result has been published by which author. I can't find a scientifical sound.

Reply 12: We have re-worded this section on the MoST technique. The first paragraph is a description of the surgical approach. The second paragraph begins with the series that reported outcomes on it, as well as a figure reference to the approach. We then transition into the complications profile of the surgery and a review paper published on glans necrosis.

Comment 13: In the "Results" section, lines 325-327, this sentence could be removed or placed in the "Discussion" section. It disrupts the presentation of the results.

Reply 13: This has been moved from the results to the discussion.

Comment 14: In the "Results" section, what is the meaning of "5 patients (1%) exchanged MPP for IPP" in line 350?

Reply 14: We did not feel that this contributed value and removed this comment. We reworded the prior sentence on complications.

Comment 15: In the "Results" section, lines 378-391, it is completely wrong to place the author's experience in the results section of a systematic review without separating it.

Reply 15: We have moved this out of the TEP results portion, instead this is now in the discussion.

Reviewer F

Excellent review-well-written and thorough. I have no suggestions to improve the manuscript.

Reply: We appreciate you taking the time to review this manuscript, we hope you are equally satisfied with the revisions suggested by the other reviewers.

Reviewer G

I want to commend the authors for an admirable job in synthesizing the literature on existing techniques for penile length preservation with IPP. There are numerous techniques, with newer published every year, as alluded to by the recently described auxetic expansion.

There are some major content-based flaws however, that should be addressed. As a whole, the manuscript needs to be reworked but has potential.

Comment 1: The paper does not make distinction between adjunctive procedures for Peyronie's disease vs. penile shortening from other pathology. The mechanism of penile shortening, corporal tethering, corporal fibrosis, etc. is v different, and as such certain techniques (for ex. modified TEP overlying plaque) would be preferred for patients with Peyronie's disease than other techniques. As such, the paper should focus on either therapies for patients with Peyronie's or other underlying pathology, or organize the manuscript between techniques that can be used in Peyronie's patients and those preferred for other patients.

Reply 1: We appreciate the feedback on the paper. The topic of the paper is to review current options available for concurrent Penile Lengthening Procedures with Penile Prosthesis. While we agree that there are many different procedures for Peyronie's disease and lots of approaches that can augment the various etiologies, this was not the purpose of the review. In the introduction, we do discuss initial surgical management of Peyronie's disease because these patients are the majority of patients included in all of the cohorts reviewed. We do discuss in the methodology in the introduction now "Regardless of the pathophysiology leading to the need for PP, we aim to review and provide an update on the expanding literature regarding techniques to preserve and enhance penile length with PLP during PP". It is important

to understand that the pathophysiology by which the patient got to the penile prosthesis may be different, but the ultimate details and the manuscripts reviewed are outlining the concurrent penile lengthening in the setting of prosthetic placement. We did not control the patient populations within each cohort reviewed, but need to address them as published.

Comment 2: Line 77 stating men who present for PLP overestimate normal penile length needs a reference.

Reply 2: We added a reference for this.

Comment 3: Line 81 stating Peyronie's disease a/w ED is ONLY scenario where PLP is accepted is, again, false, as penile shortening and tethering can be seen in multiple pathologies and should be treated if patients so desire.

Reply 3:We deleted the word only and changed it to "a", the sentence now reads: "PD with associated ED is a scenario where PLP is currently accepted as a treatment option, yet even in those cases there is no consensus on the optimal procedure amongst the experts [12, 13]."

Comment 4: Inclusion of preoperative and postoperative protocols at the start of the manuscript takes attention away from the individual techniques. VED, penile stretching, etc. should be described as ways to augment PLP and should follow a discussion of the existing PLP techniques.

Reply 4: We moved the commentary on the pre-operative and post-operative protocol to after the discussion of existing PLP surgeries. We now comment on them as ways to augment the surgery.

Comment 5: Lines 217-219. What is the difference between technique 1 and 3? Maximizing corporal length would also enhance true penile length. The subsequently described techniques are then not organized based on the breakdown listed in these lines.

Reply 5: We have removed these lines to avoid confusion.

Comment 6: Please explain the benefit of tachosil grafting over tunical incisions for TEP. Is there any concern for tethering to Buck's during postoperative healing?

Reply 6: It would be premature to have direct explanation of benefit as this has not been published. We do mention the thought process it has in helping reduce post-operative bleeding and provide additional shaft support, we are talking anecdotally about our experience by saying "We also cover our tunical incisions with 1 or more Tachosil grafts (Baxter Healthcare, Deerfield, IL, USA), to reduce post-operative bleeding

and provide additional shaft support during the healing phase." We have not seen tethering of the graft in post-operative follow-up. (Lines 448-450)

Comment 7: Why do the authors inject papaverine in both NVB and corpus spongiosum if they do not perform urethral mobilization at the time of TEP?

Reply 7: We have adjusted the information as follows to further clarify: "We are now injecting diluted papaverine into the glans, proximal corpus spongiosum, and at the base of the penis dorsally near the NVB to enhance blood flow to these structures and to reduce the risk of distal ischemia. The use of papaverine injection was a modification of technique suggested by Dr. Egydio to attempt to vasodilate the vasculature in the structures supporting blood flow to the glans and thereby reduce the most dreaded risk of glans ischemia. We recommend doing this in addition to our modifications to only elevate Buck fascia and NVB to correct dorsal and dorso-lateral curves, or the urethra and leave the NVB in situ for ventral deformities. Again, we do not recommend elevating both structures." (Lines 455-462)

Comment 8: The discussion of auxetic expansion should be moved to discussion as this is predominantly an experimental technique with no significant patient safety and long term data.

Reply 8: While patient safety and long-term data may be lacking, this was a published manuscript that fit our review paper concept. We added clarifying statements on its current role, but moving it to the discussion would not allow for the same format regarding different procedures with the previous study referenced. It would also distract from other points made in the discussion. Clarifying statement included the following "However, until more data is released on this largely experimental technique, implementation of this approach should be used with caution."

Comment 9: Discussion could be more substantial.

Reply 9: We have added much details into our discussion. We moved our experiences with the TEP approach into this part of the paper. Additionally, at the request of another reviewer we have added data on different prosthetics available on the marketplace.