Peer Review File

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Reviewer A:

The authors present a well written and research systematic review of sexual dysfunction following anterior urethroplasty. They should be commended for tackling an important issue with an article that will help with counseling our patients. There are frequent grammatical / verbiage errors throughout that require close examination and correction to improve the readability of the article. I marked some but not all below.

Comment 1: Introduction:

Line 67—is it supposed to read 45.47 years? The mean should be a single number not a range. Is the number in the parentheses the range? If so, please label it as such.

Reply 1: Changed mean age for a single number, and labeled the range in the parentheses.

Changes in the text: a mean age of 46 years (range 1-85)

Comment 2: Line 72, I believe that there is a missing word in this sentence. Perhaps "…with PROMs having been developed…"

Reply 2: It was a spelling mistake.

Changes in the text: Recently, interest has shifted towards patient satisfaction. Patient-reported outcome measures (PROMs) have been developed for addressing both micturition and sexual function.

Comment 3: Methods:

Line 97—the sentence may be more clear if you add an "An" at the start of it.

Reply 3: added "An" at the start.

Changes in the text: An additional 14 articles were included

Comment 4: Were articles eliminated after evaluation by two independent authors or by a single one? Were only the initial reviewers involved in the data extraction? If one author felt the study should be included and the second disagreed, who cast the deciding vote?

Reply 4: Two independent authors screened articles for inclusion. In case of disagreement, a third author would decide whether the study should be included. Data extraction was carried out by the two initial reviewers.

Text: Our initial search found 141 articles (Figure 1). The titles and abstracts were screened by two independent authors and 48 articles were selected for potential inclusion. An additional 14 articles were included from searching the references of the selected articles. Full text articles were retrieved for all selected references. After independent review, articles were excluded if they did not meet inclusion criteria or did not contain relevant information on the topic. In case of disagreement, a third reviewer would decide whether the study should be included.

Finally, 38 articles were included. Data extraction was done independently by two reviewers.

Comment 5: Review:

Throughout the review section, it may be helpful to include the time points for when the questionnaires were given. This was done occasionally and may be challenging to ascertain from some of the studies; however, it seems that much of the sexual dysfunction is transient and resolves within 6-12 months.

Reply: time points have been introduced for the time of the evaluation.

Line 264—it may be easier to describe this as a comparison of men who underwent EPA for short or long strictures. As it is, the sentences is a bit confusing.

Reply 5: the text has been rephrased to make it more understandable.

Text: Morey et al (26) presented a series of 22 men who underwent EPA for short (< 2.5cm) or long strictures (>2.5cm). An EF questionnaire was administered at 6 months postoperatively. Men in the longer stricture group had no increased rate of stricture recurrence or erectile complaints compared to men with shorter strictures. Erections were moderate or very satisfactory in 55.6% in the short stricture group and in 83.3% of longer stricture group ($p > 0.3$). Complete loss of erections was reported in 2 patients from short stricture group and in none of >2.5 cm

Comment 6: Line 268—should be moderate not moderately.

Reply 6: changed.

Text: were moderate or very satisfactory

Comment 7: Line 271—"associated with" not "associated to"
Reply 7: changed
Text: associated with bulbar

Comment 8: In the D'hulst et al study, were the remaining 24 patients not sexually active at time of postop evaluation or did they have severe ED leading to inability to participate in sexual activity?
Reply 8: Only 23 of the 47 patients were sexually active before surgery and completed the IIEF-5 questionnaire. I rephrased the text to clarify it.
Text: Only 23 patients were sexually active before surgery and completed the IIEF5 questionnaire

Comment 9: It may be interesting to mention the VESPAR trial which is prospectively comparing EPA vs ntEPA. I believe that sexual function questionnaires are being given to the enrolled patients. https://pubmed.ncbi.nlm.nih.gov/32917251/
Reply 9: I agree; this trial will shed light on the debate of whether non transecting urethroplasty is non inferior to EPA regarding surgical results but also on the functional benefit of bulbar artery preservation.
Text: Non-transecting techniques seem to diminish vascular damage secondary to EPA repairs, but their clinical benefit over EF are yet to be consistently proven. There is an ongoing prospective, multi-center, randomized, non-inferiority trial, comparing transecting and non-transecting techniques (38). This study will provide evidence on both surgical and functional results after these techniques, including erectile function, and will try to shed light on the value of bulbar artery preservation.

Comment 10: Line 306—vasculature not vascularization
Reply 10: changed
Text: may benefit from maintaining the urethral vasculature intact.

Comment 11: Regarding the Spencer et al study (line 315), was there a difference / any reason that the 21.4% patients with a reduction in SHIM score experienced it?

Reply 11: they do not mention any. The number of patients is insufficient to make a comparative analysis.

Comment 12: Regarding the Kessler et al study (line 322), the sexual function was significantly worse in this study compared to the other studies presented in the review. Is there any recognized reason for this? Is it how they were asking the questions since it was not a validated questionnaire?
Reply 12: Certainly, there is a strikingly high proportion of sexual impairment, specially after EPA. However, there is no recognizable reason for this through the text. It is true that patients are questioned about their preoperative sexual function postoperatively on a recall basis. In addition, the degree of impairment is graded in a little / moderate/ marked impairment, which is a subjective measure. But even taking this into account, we find it difficult to explain why the sexual dysfunction they report is so much worse compared to other studies on the field.

Comment 13: Throughout section 3.1, articles before words (a, an the) are frequently missing.
Reply 13: the text has been revised, introducing the missing articles when detected.

Comment 14: Line 385—Posteriorly?
Reply 14: changed text, that was a literal traduction from authors native language.
Text: Later, Fredrick et al (39) designed a comparative

Comment 15: Line 411, 412—are the numbers in parentheses the interquartile range or the overall range?
Reply 15: although it is not clearly stated in the original paper, I believe it is a range (MSHQ -EJS score varies from 1 to 15 maximum).
Text: improved from 8 (range 4-13) preoperatively to 11 (range 4-15) postoperatively

Comment 16: Line 458—Palminteri not Palmintery
Reply 16: corrected.

Comment 17: Line 573—the % of patients with no glans tumescence increased from 6

weeks to 6 months? (Beysens)

Reply 17: Yes, they describe an increase from 6 weeks to 6 months. However, it must be noted that fewer patients fill in the questionnaires at the second time point (20 patients vs 11 patients), so there might be a selection bias.

Text: Of 20 patients with IIEF5 $\geqslant$ 20 at 6 weeks, 10% AU and 40% augmentation patients reported no glans tumescence ($p = 0.303$). At 6 months, 16.7% (1 of 6 patients) AU and 60% (3 out of 5) augmentation patients, reported no glans tumescence ($p = 0.242$).

Comment 18: Line 574-576—this sentence is unclear.

Reply 18: It has been rephrased

Text: Although changes in genital sensitivity were not significantly different among subgroups, it is remarkable that augmentation urethroplasty patients reported a higher rate of sensitivity changes at 6 weeks (66.7% vs 53.3% in AU group). The authors attribute these…

Comment 19: Conclusions:

Please re-write the conclusion section with a native English speaker reviewing it.

Reply 19: Conclusions have been rewritten and reviewed.

Text: It is well proven that anterior urethral surgery can have consequences over sexual function, affecting erection, ejaculation and/or genital sensitivity. Sexual health is an important issue for patients undergoing urethral reconstruction. Deterioration of sexual function may cause postoperative dissatisfaction, even when a patent urethra is achieved. Penile urethra interventions, long panurethral urethroplasties, and revision surgeries pose the greater risks.

The functional benefit of non-transecting approach and grafting techniques in bulbar urethra remain controversial when compared with EPA. Prospective well designed and conducted studies are required to clarify those aspects.

Pre- and post-operative evaluation of sexual function using validated tools is of outmost importance. It can provide objective information for adequate preoperative counselling, outcome evaluation and early complication detection.

Comment 20: Table2 :
Line: Sharma et al—pendulous is misspelled
Reply 20: Corrected
Text: Pendulous

Comment 21: Bibliography:
Please rename this: References
Please ensure that journal names are written per standards
Reply 21: Renamed References.

Reviewer B:

The authors present a meta-analysis looking at all aspects of sexual dysfunction which may result from anterior urethral reconstruction. It is evident that a great amount of work went into collecting and summarizing all of this data. It seems quite ambitious, however, to review so many different outcomes for a set of surgical techniques which are already very heterogenous in nature (penile vs bulbar, transecting vs non-transecting, grafted vs EPA, muscle sparing vs not, etc.). This leads to a review article which is very long and detailed but that does not allow us to draw any evident conclusions.
Reply: Our aim was to summarize all the possible sexual health issues after to urethral surgery. It is certainly ambitious, but we believe it allows a comprehensive knowledge on the theme. It also shows the heterogeneity of the data, which makes it difficult to compare results among the studies. That should draw attention to the fact that validated tools should be used routinely in order to respond to controversial questions regarding sexual function after different procedures.

Comment 1: It is already known that anterior urethroplasty may result in transient and, rarely, permanent loss of erectile function, and this to a variable degree. There are already a number of publications on the subject, including some meta-analyses. What

is lacking in current literature is concrete information on the mechanism of action of post-urethroplasty ED.
Reply 1: We completely agree with this.

Comment 2: A recent meta-analysis on ejaculatory function post anterior urethroplasty was already recently published in the Journal of Sexual Medicine with similar conclusions as presented by the authors (Kaluzny et al.)
Reply 2: This recent systematic review agrees with the authors in the difficulty of evaluating ejaculatory function due to data heterogeneity and the use of non-validated questionnaires. The prevalence of pre-operative ejaculatory dysfunction is greatly variable when reported, and it may improve after surgical reconstruction.

Comment 3: A true discussion section is lacking. The authors present a series of sub-reviews with independent conclusions throughout the text, and each of these topics could likely have been treated as a review of their own.
Reply 3: The authors aimed to investigate the different aspects of sexual dysfunction in this review, but also believed it would be much clearer to review each topic separately in different sections.

Comment 4: The results section and the summary tables lack succinctness and synthesis
Reply 4: The authors agree tables were too condensed and they have been fully revised.

Comment 5: There are a number of grammatical, punctuation and syntax errors throughout the text which turn the attention away from the content of the manuscript
Reply 5: Manuscript has been revised to correct linguistical errors.

Comment 6: Abstract
44 « was found » and not « were found”
Reply 6: corrected

Comment 7: 46 period instead of coma punctuation after “dysfunction”
Reply 7: corrected.

Comment 8: 46-47 please rephrase sentence which begins with “appearance”, for example “Patient perception of sexual impairment was related to post-operative satisfaction

Reply 8: rephrased

Text: Patient perception of sexual impairment was related to post-operative satisfaction.

Comment 9: 43-47 the authors change verb tenses from past to present which should not be done, suggest rephrasing sentencing

Reply 9: Rephrased

Comment 10: Introduction

67 Please rephrase the sentence “According to recent European 67 studies, it affects a wide range of male population, with a mean age of 45-47 years (1- 68 85) (2, 3)” for example, “according to recent European studies, urethral stricture disease affects men of all ages, with a mean age at diagnosis of 46 years”

Reply 10: Rephrased.

Text: According to recent European studies, urethral stricture disease affects men of all ages, with a mean age at diagnosis of 46 years (range 1-85)

Comment 11: 71 Please rephrase “Recently the interest shifted towards patient’s 72 satisfaction, with patient-reported outcome measures (PROMs) been developed for 73 addressing both micturition and sexual function (5).” For example “Recently, interest has shifted towards patient 72 satisfaction. Patient-reported outcome measures (PROMs) have been developed for 73 addressing both micturition and sexual function (5). “

Reply 11: Rephrased

Text: Recently, interest has shifted towards patient satisfaction. Patient-reported outcome measures (PROMs) have been developed for addressing both micturition and sexual function

Comment 12: 78 please revise the objective of the study as the sentence is not clear “The aim of the present review is to summarize the impact of male anterior

urethroplasty 79 surgery over the sexual health." What does "over the sexual health" mean? Your described aim in the abstract is much clearer than in the text

The authors should describe in the introduction which specific sexual dysfunction outcomes they will be investigating in their meta-analysis, as this will shape their methods and key search words in the subsequent methods section

Reply 12: the aim of the study has been rephrased so it is more clearly defined.

Text: The aim of the present review is to summarize the impact of male anterior urethral reconstruction over postoperative sexual function, including erectile function, ejaculation, penile size, penile curvature, and genital sensitivity. Possible factors predicting sexual outcomes were additionally discussed.

Comment 13: Methods

83 suggest "prior to" instead of "before"

Reply 13: corrected

Text: The inclusion and exclusion criteria were determined prior to the literature search.

Comment 14: 89 syntax error, please correct "comprised only of"

Reply 14: corrected

Text: The eligibility criteria are comprised of English-language studies, on male patients older than 18 years old, who underwent any type of anterior urethroplasty.

Comment 15: 93 remove hyphens in "pelvic fracture related"

Reply 15: corrected

Comment 16: 112 delete the word "such"

Reply 16: removed

Comment 17: Figure 1. change "2 study" to "2 studies" and remove coma after "Full text articles excluded" in its box

Reply 17: Corrected.

Comment 18: Results

129-132 These statements need a reference

Reply 18: the reference has been introduced.

Text: Mundy et al were the first to report ED after urethroplasty in 1993. He described a 5% permanent ED after anastomotic urethroplasty (AU) and 0.9% after patch urethroplasty in a series of 200 patients(7).

Comment 19: The standardized questionnaires are explained in detail, but this is not necessary within the text. They can be put in an Appendix

Reply 19: Authors believe a little explanation might be helpful; however, the section has been reduced.

Text: - International Index of Erectile Function (IIEF)(9): validated self-administered 15-items questionnaire evaluating 4 domains: erectile function (Q1-5, Q15), orgasmic function (Q9-10), sexual desire (Q11-12), intercourse satisfaction (Q6-8) and overall satisfaction (Q13-14). Each question is answered in a 0-5 scale, to a maximum of 75 points.

- Sexual Health Inventory for Men (SHIM or IIEF5): modified 5-item version of the IIEF, designed to assess the presence and severity of ED according to specified benchmarks.
- O'Leary Brief Male Sexual Function Inventory (BMSFI)(10): A 11-question questionnaire that rates from 0-4 the following items: sexual drive, EF, ejaculation, problem assessment and overall satisfaction. There are no defined benchmarks for this questionnaire, so it is difficult to state the clinical relevance of a certain decline.
- Male Sexual Health Questionnaire (MSHQ)(11): 25-item self-administered questionnaire that evaluates erection, ejaculation, and satisfaction. Some authors used ejaculation items as an independent questionnaire, as it provides a detailed evaluation of the topic (MSHQ-EjD).

Comment 20: There are various syntax and grammatical errors throughout the results section and in the conclusion. This should be revised to ensure a high-quality manuscript.

Reply 20: The whole manuscript has been revised to try and correct the grammatical errors.

Comment 21: Tables

The tables are very busy and have a lot on information on them, which makes them strenuous to read, notably the “results” sections.

Reply 21: Tables have been revised and result section simplified.