Peer Review File

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Reviewer A

Lines 40-42
Comment 1: should there be an "and" following to word "nares"?
Reply 1/Changes in Text: Changed “Aside from pre-surgical scrub, use of mupirocin and chlorhexidine have been implemented for 5 days prior to surgery and shown to treat *Staph aureus* colonization in the nares and to decrease surgical site infections.” Added and changed wording for clarity.

Comment 2: please specify the type(s) of surgery being assessed in these studies. Should be clear to the reader that this is not IPP-specific data.
Reply 2/Changes in Text: “These studies were largely from orthopedic surgery, general surgery and neurosurgery cohorts.” Added line to discuss study populations.

Line 250
Comment 3: "prior IPP placement" could refer to a patient who is undergoing an IPP remove and replace procedure due to malfunction or could refer to a patient who has had a prior IPP explant due to infection or erosion. These populations have distinct risk profiles. Please specify what you are referring to in this section. "Prior IPP Explant" make be a more accurate title for this section.
Reply 3: added a sentence for clarity. This section primarily refers to any previous IPP placement and the risk for subsequent explantation secondary to infection in the future.
Changes in Text: Specifically, any prior IPP, regardless of infection status, predisposed patients to needing an explantation relative to IPP-naïve patients. (Line 256)

Line 280
Comment 4: should the word "surgery" follow the word "general"?
Reply 4: we were making a general statement, I removed in general to add clarity
Changes in text: Removed “in general,” (Line 282)

Lines 380-381
Comment 5: this is confusing, because the prior sentence seems to indicate that all of the patients had a neobladder. I'm not sure how they could have assessed something that every patient had as an independent risk factor?
Reply 5: omitted comment to add clarity and simply left the sentence before
Changes in text: ~~Of note, neobladder placement was noted to not be an independent risk factor for IPP infection.~~ (lines 384-385)

Lines 395 and 399

Comment 6: The author's last name is "Loh-Doyle"
Reply 6: fixed name
Changes in text: Loh-Doyle et al reviewed 78 patients who underwent 3-piece IPP placement after treatment with pelvic radiation (external beam radiation and or brachytherapy). [78] Only 2 patients in this group developed infectious complication which aligns with percentages of infection from most other studies leading these authors to conclude that IPP placement after radiation is not a risk factor for infection. Other studies support this group's findings. (lines 399-403)

Comment 6: Table 1
- I recommend breaking this up further in terms of
a) factors with evidence actually supporting the idea that they are risk factors for IPP infection vs. those without
or
b) factors with no, weak, or strong data to suggest there are risk factors for IPP infection

As it stands it's a bit odd to have the table labeled as "Infection Factors" after you've appropriately rejected the idea that many of these things are actually related to IPP infection.

General Consideration
- I would consider adding a subjective categorization to the title of each section
- for example:
-- Use of Bupivacaine - NO Evidence of Increased Infection Risk
-- Prior IPP Explant - STRONG Evidence of Increased Infection Risk

Something like this might be helpful

Reply 6/Change in text: added to Table 1 the grading of evidence, as reflected in the new version of Table 1. Given that several reviewers wanted this in the Table 1 format, this felt like the best place to put the subjective categorization. We would be happy to change the title of each section as well if you feel like both are warranted. We just didn't want to be too redundant. Additionally, changed Table 1 name.

Reviewer B

Comment 7: Really nice review.

There are a few stylistic language issues throughout the manuscript that would benefit from one additional read-through. There was a lot of excellent work put in to pull and synthesize all of the data but the person primarily responsible for doing so may need a little more assistance in communicating it according to 'standard' language.

For example: line 114 - "Another recent study utilized a 309-patient prospective

database to run statistics on the involvement of residents in IPP surgeries."

Reply 7: read through with all authors to ensure that wording was improved. Specifically changed the above sentence to read more clearly and efficiently. All of these changes have been tracked in red in the new manuscript.

Changes in text: throughout, rewording of sentences to be more concise and utilize more standard language.

Reviewer C

Comments 8: This is a scholarly work by a very reputable group with extensive experience in prosthetics, and it shows in their manuscript. They covered most of the critical aspects of surgical management of prosthetics and did a great job. The readership of TAU will benefit from it.

Replies 8:

I do have several minor comments and suggestions:
1) Table one has a typo in factors. (This was changed)
2) I do not believe Table 1 adds anything of value to the manuscript. Is present forms it lists Factors but doesn't provide the reader with whether these are modifiable, important or positive or negative. (I have modified Table 1 significantly as recommended by Reviewer A and C. These changes include important positives and negatives to grade evidence that has been reviewed in this paper)
3) They should expand the conclusion or create a summary in which they integrate their experience and knowledge and provide guidance to the reader looking to reduce their infection rates. Conclusion was significantly changed as outlined under Reviewer D
4) They provided no information of fungal infections or information on what bugs are causative of most infections and how these vary within various populations. We would be happy to include this if there is another specific paper that is desired. We had some difficulty finding significant data that addressed this in regard to the IPP population outside of the paper we had included in the diabetic section. We did add a few sentences about fungal infections in the diabetic/obese population. This is found in the diabetes section.

'Additionally, the fungal infections were commonly found to involve *Candida* species. Given that obesity and diabetes seemed to be predisposing factors for fungal IPP infections, this study concluded that patients with such comorbidities may benefit from antifungal prophylaxis.'

5) They did not address which of the available implants from the various manufacturers are at greatest risk of complications or infections. We did not find significant data that addressed differences in the main IPPs currently utilized in today's surgeries. We would be happy to include a paper over this if there is a specific paper desired.

6) They did not address intra-operative factors that can lead to infection such as urethral injury or selection of the wrong cylinder length leading to erosion, aggressive dilation leading to extrusion etc... We will plan to address this in the subsequent manuscript that has been requested by this reviewer.
7) I understand that it may be beyond the scope of the current manuscript but I would love to see a companion piece or a simultaneously submitted manuscript on management of the infected prosthesis from this group, which would in a step wise manner review the existing literature on management of the infected device and provide strategies to salvage and safely explant the devices. We will plan to email TAU and address this to write a follow up paper.
8)Finally, I would suggest the authors create a Table that unifies their findings and provides the readership with which elements have studies that support the findings and which are based on historical practices alone. (Table 1 has been significantly modified to provide better clarity in terms of elements to consider and the evidence behind them)

Reviewer D

We have addressed reviewer D's comments in our summary/conclusion section. We have discussed glove changes, preop labs, penile conditions, limited personnel, catheter placement and irrigation.

Text additions: "We present a novel narrative review that highlights many important factors to consider when addressing the risk of infection in penile prosthesis surgery. It is worth noting several techniques we utilize to reduce infection risk in patients undergoing penile prosthesis placement. Preoperatively we perform a urinalysis and culture on every patient scheduled for penile prosthesis placement. We treat any positive culture and ensure negative results before proceeding with surgery. Additionally, perioperative antibiotics are ordered in our preoperative clinic. These antibiotics generally consist of vancomycin and gentamicin.

After patient positioning, hair removal is accomplished with the utilization of a razor to avoid skin abrasions like those seen with the use of clippers. The external genitalia are prepared with a 5-minute chlorhexidine scrub followed by chlorhexidine paint preparation with 2 sticks. The chlorhexidine is allowed to dry for 3 minutes as suggested by its manufacturer. After proper draping of the patient, we immediately place a urinary catheter to emptying the bladder as our first step. We place the catheter in standard sterile fashion and we utilize a miniature chlorhexidine stick to re-prep the catheter once it settles at the bladder neck. This technique for chlorhexidine prep of the catheter is attributed to Dr. Eugene Rhee.

We utilize an antibiotic dipping solution as has been outlined in the literature. [17] Vancomycin and gentamicin has been shown to be the most efficacious combination and the most commonly used. We use our solution to submerge instruments before using them and to bathe components of penile prostheses before implantation. Additionally, we use our solution to wash our hands between steps. Finally, we use our solution in a bulb irrigator to rinse the penile prostheses as they is being placed. Double-gloving is always utilized during penile prosthesis placement at

our institution and the outside gloves are changed before and after steps that involve manipulation of the prosthesis.

In general, we limit penile prosthesis cases to one surgeon and two residents at maximum. Additionally, we only have on scrub tech and one circulating nurse and on anesthesia provider once the prep of the patient has occurred and no one is to enter or leave the room.

Strides have been made since the initial penile prosthesis surgeries to improve infection rates including diabetes control, antibiotic coating of devices, and antibiotic implementation. Going forward, more studies, especially randomized control trials, need to focus on defining levels of diabetic control (sugar control and A1C control), determining the role of metabolic syndrome in infection promotion and determining laboratory values which could be predictive of infection."

1) Please elaborate as to if any pre-op labs or urine cultures were taken
2) were there any glove changes?
3) What was the status of pre-existing penile conditions e.g. fibrosis, Peyronie's, or penile fractures? Did incidence increase infection?
4) Was there a limit on personnel in the operating room?
5) Elaborate on catheter placement methods and duration
6) irrigation method at time of placement?

Reviewer E

The authors should be commended for the work on "Penile Implant Infection Factors: A Narrative Review of Literature". The manuscript is clear, concise and a joy to read. The manuscript would be enhanced if the authors included a table with the highlights of each Implant factor. (Table 1 has been modified to include implant factors and the evidence grading which backs the factor)

Reviewer F

I congratulate you to review this complex subject. And the systematic way you addressed each point with the current recommendations.

Thank you for your review

Reviewer G

Authors provide a comprehensive review of risk factors for penile implant infection. The manuscript would benefit from three items to improve the quality and readability.

1) An improved description of the methods. What years were manuscripts taken. How many were reviewed. Why were some selected and some removed, etc.

2) Many reviews like this exist with a 1-2x new ones each year. This manuscript does include new items, such as phalloplasty and use of local analgesics... Perhaps the authors could rank the most significant causes of infection...this would make this manuscript unique compared to others. (Table 1 has been altered significantly to address more of a ranking or grading so to speak in terms of grading of evidence into strong, intermediate, weak and no evidence categories.)

3) It would be helpful to have a summary table for all the factors evaluated and whether the factor is risk factor for infection, protective against infection, or does not matter. Including the level of evidence would also be great. (This has been addressed as above in table 1 and throughout the manuscript)

Minor edit - Figure 1 spelling of "Factors" (Fixed)

Reviewer H

The authors present a very detailed and well labored review of the current literature on penile prosthesis infections and risk factors. This topic is one that already has a variety of review articles even from the last two years. While detailed, the review is rather limited in its formatting and continuity of outcomes. Furthermore, their description of a multitude of risk factors favors a width of review while sacrificing depth. While this is not a formal systematic review, there are still many important PRISMA check boxes left unaddressed (only a truncated version appears attached to this draft). An assessment of strengths and weaknesses of most of these studies should be included and this may require narrowing the scope of review at the expense of sections like climate. Alternatively, providing more detail to the less commonly addressed topics such as climate by sourcing from other orthopedic or non-urologic literature would make this review more novel.

Overall, major revisions are recommended prior to publication. The review needs to include at least some assessment of the strengths and weaknesses of referenced studies and provide some novelty and commentary to the review.

More discussion has been added throughout; additionally, Table 1 and headings have been altered to reflect a better appraisal of evidence.