Peer Review File

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Reviewer A

1. Methods

- Specific definitions and number of patients for each group are missing.

Definitions of each arm are mentioned in the Methods section. On page 6, lines 17-19 under the <u>Study Design and Population</u> header, we define the control arm. The intervention arm is described in the Methods section, under the <u>Study Design and Population</u> header on page 6, lines 14 and 15 with further description in the Methods section, under the <u>Intervention</u> header on page 7, lines 4-9

- How many surgeons performed radical prostatectomy?

8 surgeons. We have added this in the Methods section, under the <u>Study Design and Population</u> header on page 6, lines 6 and 7

2. Table 1

- Please show the ratio of preoperative EHS 3 and 4.

Unfortunately, we did not assess EHS pre-operatively. Pre-operatively, only IIEF-5 scores were assessed.

- BMI is missing.

Unfortunately, we did not assess BMI.

- Were there any differences in Open vs Robot-assisted RP between the groups? This analysis was not performed. Most of the patients included underwent robotic prostatectomy. This comparison was not an endpoint of our study.

3. Table 2

- Please show the categorical EHS after rWT.

We added the categorical EHS in the Results section, page 9, lines 15 and 16 and added Table 3. The categorical comparison using an EHS of 3 as the cut off is similar to how Jang et al (ref #14) reported.

4. Univariate and multivariate logistic regression models for predicting the EHS \geq 3 or, IIEF \geq 17 after rWT are essential.

- It can be pointed out that this is the biggest problem in this study.

- If it is concluded that wRT is significant as a predictor of an EHS score of 3 or higher in multivariate analysis, the title may need to be changed.

We understand the reviewer's point. However, we are comparing two binary outcomes, intervention/control with erectile function recovery/lack of recovery. Further, the baseline characteristics between the two groups that we have compared are not significantly different. While a logistic regression may be helpful, we chose to use a chi-squared test.

5. It would also be good for the readers to show bar graph of gradual improvement in IIEF or EHS after rWT.

We feel that Table 2, which describes the change in median EHS and mean IIEF-5 scores suffices. Table 2 is the crux of our comparison and primary outcomes. We feel that this is more important than a bar graph.

6. Please add this reference to your manuscript.
PMID: 35347300
DOI: 10.1038/s41443-022-00560-w
We have included this reference (#14) in the Introduction section, page 4, line 15 and in the Discussion section on page 12, lines 10-16

Reviewer B

The manuscript titled as "Radial Wave Therapy Does Not Improve Early Recovery of Erectile Function after Nerve- Sparing Radical Prostatectomy: A Prospective Trial" is a prospective study about the effect of radial wave therapy for patients with nerve-sparing radical prostatectomy. In this manuscript showed that rWT had hardly advantages for the recovery of early erectile function after NS RP. It's meaningful for guiding clinical treatment. However, short-time follow-up and lack of credible control limited this study. Here are some questions author needs to address:

1. Time diagram should be added in the M&M part.

We have added a Time Diagram, called Figure, which will be attached separately. This is mentioned in the Methods section under the <u>Study Design and Population header, page 6</u>, lines 19 and 20; additionally, the Figure Legend is on Page 21.

2. PDE5I, as a parameter which largely impacted results, should be quantitative management in each group.

We agree that this measure is important. Unfortunately, given that at our institution there are many surgeons who perform radical prostatectomy and use different penile rehabilitation PDE5I dosing, we were unable to standardize the dosage. There was no significant difference in usage of PDE5I between the arms.

3. Authors said IIEF-5 and EHS surveys were performed at 6, 12, and 24 weeks postoperatively, but there were not described in results in detail.

We corrected this to 6 and 12 weeks in the Methods section, under the <u>Outcomes Measurement</u> header, page 7, line 13. In the results, we combined the 6-12 post-operative range; for those study subjects who had more than one survey result, we used the later result.

4. During the rWT, were the dose of PDE5I and rWT setting changed, if the effect was poor. Dosing of PDE5I was at the discretion of the prescribing provider, but typically is not changed. rWT settings were standardized for all treatments and were not changed if effect was poor.

5. In previous study, Baccaglini W et al were performed a randomized clinical trial in which the study was about SWT for patients with RP as well. So what's main differences. Was it just SWT changed to rWT?

Correct. There are multiple studies of fSWT in the vasculogenic ED setting and several in the post-RP setting. Still, rWT is advertised and used clinically without data that supports or refutes its use. Our study is the first to use rWT in the post-RP setting.

<mark>Reviewer C</mark>

Thank you for inviting me to review the manuscript titled "Radial Wave Therapy Does Not Improve Early Recovery of Erectile Function after Nerve-Sparing Radical Prostatectomy: A Prospective Trial." This is an important piece of research. The investigates the results obtained after the use of radial wave therapy in 106 patients following a nerve-sparing radical prostatectomy related to patients' erectile function. The study had a prospective design, which is good, but I want to raise several issues that should be clarified before publication. Overall, the methodology of the study is confusing, the paper requires substantial improvement.

Please add a few words about intervention in the abstract in methods. If there is too little room, please shorten the background, which provides some general information. Also please use a well-known abbreviation for the IIEF-5 questionnaire in the abstract.

We have added further description about our rWT intervention in the Abstract, Page 3, lines 1 and 2. We also added that abbreviation in the Abstract, Page 3 line 4 and also line 6.

Line 83. You mention 4 studies evaluating SWT in the post-RP setting. I can see only 3 – Frey, Baccaglin, and Ladegaard. Porst is a review, not a clinical trial, isn't it? Please clarify this issue. Based on Reviewer A's recommendation, we now list 5 studies in the post-RP setting (Frey et al, Porst, Baccaglini et al, Ladegaard et al and Jang et al). In his paper, Porst reports 12 consecutive patients who benefitted from SWT. While Porst's paper is not a clinical trial, we

Line 123. Please specify which of the IIEF-5 questionnaires you used? Please explain the rationale for including patients using the cut-off level of \geq 17 instead of the standard cut-off of \geq 21.

feel that it is important to cite it given the paucity of published data on this topic.

We specified the IIEF-5 we used in the Methods section under the <u>Outcome Measurement</u> header, page 7, lines 14-16.

We used an IIEF-5 score of 17 as our cut off as that is the low end of the mild ED range. If these patients undergo a nerve-sparing radical prostatectomy, along with penile rehabilitation, it is reasonable to expect recovery back to an ability to achieve erections. Further, limiting the inclusion criteria to only men with normal erections pre-operatively would have made accrual of patients more difficult. Indeed, Jang et al (ref #14) used an IIEF-5 score cut off of 15 and Baccaglini et al (ref #11) used IIEF-5 score of 18 as their study's cut off.

Line 147. The outcomes were measured at specified time points postoperatively. This is confusing as many studies evaluate the outcomes based on post-treatment time points. Comparisons between studies using differently defined timeframes are not valid. If you evaluate treatment, data should be assessed after treatment, not after another timepoint in the past. Such assessment brings little information about treatment. If a patient started 6-week treatment at week 4 and returned an IIEF-5 form at week 6 post-operatively, he had the assessment in the middle of the treatment. It doesn't make sense. Please provide the rationale for your methodology or recalculate the results.

We agree with your assessment. The mention of "4 weeks" was an error and was changed to 6 weeks in the Methods section, under the <u>Outcome Measurements</u> header page 8, line 4 and in the Results section, page 9, line 3.

In the Intervention arm, all patients initiated rWT treatment at approximately 2 weeks after surgery (as we note in the newly added Figure). All patients were sent surveys at approximately 6 and 12 weeks. Included patients had at least one survey response between 6 and 12 weeks; for those with two survey responses, the latter was used for analysis. We now indicate this in the Results section, page 9, lines 4 and 5.

Line 155. IIEF-5 score \geq 17 is not normal. Please correct according to the classification.

We edited "normal" to "near normal". This can be seen in the Abstract's Methods section, page 3, line 4, the Methods section, <u>Outcomes Measurement</u> header page 8, line 2 and <u>Statistical Analysis</u> header page 8, line 8, and in the Discussion section page 11, line 4

The manuscript is difficult to read. Some sentences are confusing and require substantial rewriting. You would benefit from the help of a check provided by a native English-speaking medical writer.

We have re-read the manuscript and corrected some grammatical errors. Further, we used Spell Check to correct any spelling mistakes. All authors are native English speakers and have reviewed the manuscript.

The reference format at the end of the paper should be checked against the journal guidelines. References are listed in the Vancouver style as is required by the TAU author guidelines