Peer Review File

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Reviewer A:

<u>Comment 1:</u> "Furthermore, we recorded the length of the patients' stay after readmittance, whether or 32 not a concomitant venous thrombosis could be found, whether or not the SLC was treated 1 via cannulation and drainage, instillation of doxycycline (including frequency and duration of 2 instillation) or LF, whether or not an antibiotic treatment was initiated, whether or not 3 another cystogram was conducted and whether or not the discharge examination by US 4 showed persistent lymphoceles (as well as their size)." - Can you please rephrase this sentence? Instead of using 'whether or not" on so many occasions.

<u>Reply 1:</u> We agree with the reviewer that this sentence needs rephrasing to be read fluently. Also, we noticed that several of the mentioned parameters were not relevant, as they did not become part of the analysis.

<u>Changes in the text:</u> We have rephrased and corrected this sentence (see page 5 lines 15-19).

Comment 2: Did you evaluate the size of the lymphocele and symptoms?

<u>Reply 2:</u> This is a correct remark by the reviewer. Unfortunately, when retrospectively reviewing the data, we found that the size of the lymphocele at the time of readmission of the patient had not been evaluated in a standardised manner and therefore could not be analysed.

Different lymphocele measurements were applied at readmission to physician's discretion (largest diameter in ultrasound imaging, volumetry in ultrasound imaging or volumetry in CT scan (not every patient had a CT scan), thus it was not possible to compare these measurements. However, the symptoms at the time of readmission of the patient (local pain upon pressure, deep venous thrombosis or signs of infection) were evaluated (see page 5 lines 9-12).

Changes in the text: We did not apply any changes to the text.

<u>Comment 3:</u> I am not sure we have to include no PLND category when comparing pathological staging of lymph nodes with symptomatic lymphocele.

<u>Reply 3:</u> We agree with the reviewer that further explanation is required with regard to PLND. In all patients who received PLND, bilateral PLND was performed which included at least the removal of the LNs overlying the external iliac artery and vein as well as the LNs within the obturator fossa cranially and caudally to the obturator nerve. A more extensive PLND was performed in case of pre- or intraoperatively suspect LNs.

<u>Changes in the text:</u> We have added this information to the manuscript (see page 4 lines 19-22).

Comment 4: Can you do a multivariable analysis. I only see a univariate analysis.

<u>Reply 4:</u> We agree with the reviewer that a multivariable analysis would help to better understand the significance of the reported results. BMI (p<0.001) as well as Gleason score (p=0.016) remained statistically significant.

<u>Changes in the text:</u> We have added the results of the multivariable analysis to the manuscript

Comment 5: Would it be possible to re-stratify patients on NCCN risk groups?

<u>Reply 5:</u> We thank the reviewer for the chance to elaborate on this remark. At our clinic the risk stratification of patients with prostate cancer is done into low-, intermediate- and high-risk (as recommended in the EAU and S3 guidelines), using clinical tumour stage, PSA level and Gleason score. Therefore our retrospective data collection did not comprise the PSA density, the prostate gland size or the number of positive biopsy cores, which is why a restratification of patients in NCCN risk groups is not possible.

<u>Changes in the text:</u> No changes to the text have been applied.

<u>Comment 6:</u> I think the authors must restructure table 3. I do not understand why are there two successfully treated columns. How are the percentages calculated? Shouldn't the percentage be calculated with overall number. Personally, I would remove the row on successfully treated below.

<u>Reply 6:</u> We thank the reviewer for pointing out that this table needs further clarification. We wanted to show the number of successfully treated SLC per therapeutic option (drainage, instillation, surgery) on the right, calculated as "SLC successfully treated with X" as a percentage of "all SLC treated with X" (as a total of 102 SLC cases received drainage, 56 SLC received instillation and 54 SLC received surgery). In the last row we wanted to show the number of successfully treated SLC cases per treatment algorithm, although we agree that this information might be redundant.

<u>Changes in the text:</u> The last row on successfully treated patients was changed to simply show the total number of SLC cases per treatment algorithm (see page 19, table 3, "SLC cases").

Comment 7: What is the inference of table 4. It does not add anything to the conclusion.

<u>Reply 7:</u> We agree that an explanation of this table's contribution to the manuscript is needed in the conclusion. We wanted to show that most of the isolated bacteria from SLC are commensal with low pathogenic potential and an infected SLC with pathogenic bacteria is not a frequent complication.

<u>Changes in the text:</u> A sentence concerning the above mentioned statement from table 4 has been included in the conclusion (see page 11 lines 6-7). Also, a reference to the table has been added to a matching statement already in the manuscript (see page 10 line 23).

<u>Comment 8:</u> With only 13 patients I am not sure if you can conclude that laparoscopic fenestration should be used as the first line? May be an additional cost benefit analysis would help so that one can quantify benefit.

Reply 8: We agree with the reviewer that this number of patients is too low to draw any definitive conclusions. Overall, there were 54 patients treated with laparoscopic fenestration, either treated by solely fenestration or following drainage or following drainage and instillation. In 53/54 cases laparoscopic fenestration was the last and thus most efficient treatment. This brought us to change clinical routine at our hospital. Since 2018 we are performing laparoscopic fenestration as the first and definitive treatment in symptomatic lymphoceles at our hospital without any recurrent lymphocele. In addition to a cost-benefit-

analysis certainly larger prospective studies are needed to further confirm these findings.

<u>Changes in the text:</u> The text has been altered accordingly (see page 11 lines 7-11), also the abstract (see page 2 line 23). Also, this statement could be found twice in the discussion section. The first redundant version was removed from the manuscript (see page 10).

Comment 9: There is no conclusion in the paper.

Reply 9: We thank the reviewer for pointing this fact out to us.

<u>Changes in the text:</u> A conclusion has been added to the discussion section (see page 11 lines 4-11).

Reviewer B:

<u>Comment 1:</u> RARP--> Robot-assisted radical prostatectomy.

<u>Reply 1:</u> We agree with the reviewer that the manuscript can be read more fluently when using "prostatectomy" instead of "prostatovesiculectomy".

Changes in the text: We have applied this change to the manuscript (see page 2 lines 3 and 8 as well as page 3 line 9). We have also applied this change to the title as well, to "Epidemiology and therapy of symptomatic lymphoceles after robot-assisted radical prostatectomy (RARP)". If the editorial board should not agree with the change of the title, the original title can be used.

<u>Comment 2:</u> In the introduction, the authors claims that RARP offer a better oncological and functional outcome which is not true and contradict with reference number 5.

<u>Reply 2:</u> We thank the reviewer for noticing this mistake.

<u>Changes in the text:</u> This sentence in the manuscript has been corrected (see page 3 lines 10-12).

Comment 3: Reference number 5 need to be cited properly.

Reply 3: As above, we thank the reviewer for noticing this mistake.

Changes in the text: The citation has been corrected (see page 3 lines 11-12). Also, we noticed a mistake concerning the authors in citation 4, which has been corrected as well (see page 14 line 12).

<u>Comment 4:</u> What was the indication to do lymphadenectomy? Did the authors use nomograms? What is the limit of their PLND? Any patient had ePLND?

<u>Reply 4:</u> We agree with the reviewer that further explanation is required with regard to PLND. In all patients who received PLND, bilateral PLND was performed which included at least the removal of the LNs overlying the external iliac artery and vein as well as the LNs within the obturator fossa cranially and caudally to the obturator nerve. A more extensive PLND was performed in case of pre- or intraoperatively suspect LNs.

<u>Changes in the text:</u> We have added this information to the manuscript (see page 4 lines 19-22).

<u>Comment 5:</u> What is the adopted technique to do PLND? Do the authors used titanium clips, monopolar, bipolar, or any hemostatic agents/sealant?

Reply 5: We thank the reviewer for pointing out to us that this sentence is in need of further

explanation. The lymphatic vessels were sealed by bipolar cauterisation, clips were placed in addition according to the surgeon's preference. No hemostatic agents were applied.

Changes in the text: The manuscript has been changed accordingly (see page 4 lines 22-23).

<u>Comment 6:</u> The impact of Pelvic drain on lymphocele formation is not clear in the literature. What is the % of pts with pelvic drain?

<u>Reply 6:</u> We thank the reviewer for pointing out to us that this sentence is in need of further explanation. At our clinic all RARP patients receive a pelvic drain. The time of postoperative removal of the drain depends on the drain output (median: 2 days).

<u>Changes in the text:</u> The explanation has been added to the manuscript (see page 4 lines 29-30).

<u>Comment 7:</u> LMWH has been implicated in forming LC. What is your DVT prophylactic protocol?

<u>Reply 7:</u> We agree with this important advice from the reviewer that the DVT prophylactic protocol should be included in the manuscript. At our clinic all patients receive a daily dose of 5000 IE of LWMH for four weeks postoperatively. Patients with atrial fibrillation or a history of DVT or pulmonary embolism receive a therapeutic or half-therapeutic weight-adapted LWMH dose according to their CHADS-VASc-score.

Changes in the text: This explanation has been added to the manuscript (see page 5 lines 4-7).

<u>Comment 8:</u> What is the difference in the population who had asymptomatic lymphocele and those who had SLC?

<u>Reply 8:</u> We agree with the reviewer that this would be an interesting analysis. However, as this study is a retrospective data analysis, we have no conclusive follow-up on asymptomatic patients. Asymptomatic patients are not routinely seen in our hospital as they are followed-up in an outpatient setting in Germany. The SLC patients from this series were readmitted to our hospital, which is why we could collect follow-up data. Therefore, a comparison of asymptomatic LC patients and SLC patients in this study is not possible.

Changes in the text: No changes to the text have been applied.

Comment 9: Definition of treatment success is obscure.

<u>Reply 9:</u> We agree with the reviewer that treatment success need to be defined precisely. Any therapeutic approach used to treat a case of SLC was defined as successful if the patient did not experience a recurrence and did not require further treatment.

<u>Changes in the text:</u> A statement regarding this definition had originally already been included in the results section (see page 7 lines 3-5). However, to make the definition clearer, we now have also included this statement in the methods section (see page 5 lines 20-22).

Comment 10: Discussion is redundant with no clear message.

<u>Reply 10:</u> We agree with the reviewer that without a conclusion at the end the discussion section lacks a clear message.

<u>Changes in the text:</u> A conclusion has been added to the discussion section (see page 11 lines 4-11).