

Peer Review File

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Reviewer A

There are several revisions and annotations to answer before this article should be considered for publication. These are my comments:

- One of the strength of this study is the long follow up. As it has been published before, most of the (symptomatic) lymphoceles occur in the first 90 days postoperatively. Unfortunately, the authors did not state, how many lymphoceles occurred in which period postoperatively (30 days, 90 days, 180 days and so on). This should also be discussed whether longer follow ups than usual are useful.

Reply 1: We thank the reviewer for their in depth review of our manuscript. We added to our manuscript the categorized time to event data. Interestingly, half of the patients presented after 90 days and one-third after 180 days, making a strong argument for long follow-up.

Changes in the text: line 181 added: Of those 30, 9 patients presented within 30 days, 6 patients between 30 and 90 days, 5 within 90 and 180 days, and 10 patients later than 180 days.

Line 46 added: one-third of SLCs presented after 180 days.

- L37 ff. the definition of SLC should be described in the abstract

Reply 2: We thank the reviewer for pointing out this remark.

Changes in the text: We added in line 31: “lymph fluid-filled collections within the body lacking epithelial lining.”. And line 33: In this study we investigate the incidence of imaging confirmed symptomatic lymphoceles (SLC) in a centralized high-volume operating centre and assess predictive factors and treatment.”

- L31 ff. Do you mean lymphoceles in general or symptomatic lymphoceles?

Reply 3: In the first line we mean general, all lymphoceles. We sketch an overview of the topic at hand. Later we clarify our specific research subject entails symptomatic lymphoceles; which we added to the text.

Changes in the text: Line 33: In this study we investigate the incidence of imaging confirmed symptomatic lymphoceles (SLC) in a centralized high-volume operating centre and assess predictive factors and treatment.

Who assumes that the incidence of lymphoceles is 1-2% postoperatively after RARP? Are there studies that support this assumption? In the literature there are several (prospective) studies that demonstrate higher incidences than 1-2% with shorter follow up than in this present study, both for asymptomatic and symptomatic lymphoceles. A symptomatic lymphoceles rate of 7.4 % is therefore not a novelty, but only confirms the findings already published.

Reply 4: We thank the reviewer for this feedback. With a broad SLC definition (imaging confirmed lymphoceles with symptoms, not only invasively but also conservatively treated), and

a longer than usual follow-up we aim to bring novelty. The 1-2% mentioned in our manuscript was based on an older study from another centre in the Netherlands (Van der Poel et al. K Endourol 2012; 26: 1618-1624). In the revised version of our manuscript, we have rephrased this paragraph and specifically excluded the 1-2%.

Changes in the text:

Line 35: ~~At a high volume operating centre, where follow-up was decentralised, surgeons assume an incidence of 1-2% which we hypothesize to be an underestimation.~~

Line 50: ~~There was a discrepancy between the incidence we found in this study and the surgeons' expected incidence of SLCs, presumably due to decentralized follow-up, suboptimal registration and late symptomatic presentation.~~

line 96: The reported incidence on SLC varies from 0-12%, with recent studies focussing on operating techniques reporting incidences toward the upper end of the spectrum (2, 9-11).

Line 103: In this study we investigate the incidence of SLCs in a centralized high-volume operating centre and assess predictive factors and treatment, both conservative and invasive.

Line 304: In this retrospective cohort study we identified an SLC incidence of 7.4%. Many patients presented later than the centralized surgeons' postoperative follow-up. ~~which could in part be explained by its rather late presentation after surgery and decentralised follow-up.~~

- Is it correct that of the 8 hospitals mentioned, data from 3 hospitals were used? This should be described more clearly in the methods section.

Reply 5: This is indeed correct. We have described this in line 120: "We analysed the data of patients whose records were available either at the EMC, MSH or SFG for complications. These three centres were selected taking into account study feasibility and representability."

Changes in the text: -

- The follow-up process, on the other hand, should be described in more detail. How did the data come about? Was there a time (e.g. one year after the operation) when the data was followed up?

Reply 6: Patient records were analysed on a specific time point, namely Nov-22 and Dec-22. Patients had standardized moments of follow-up.

Changes in the text:

line 119, added: "Between November and December 2022...."

Line 122 added: "Postoperative follow-up was performed by the centralized surgeons after 6 weeks. The referring urologist continued follow-up after 4 months, 3-monthly in year 1, 6-monthly in year 2 and yearly from year 3."

How was the diagnosis of symptomatic lymphocele made? Was the lymphocele detected sonographically or CT morphologically?

Reply 7: This is explained in line 153 "Diagnosis of an SLC, ~~supported by symptoms of postoperative abdominal/leg pain, thromboembolic events or fever,~~ was registered if confirmed by ultrasound, CT, or magnetic resonance imaging. Imaging was not routinely performed, but only if there was clinical suspicion of an SLC due to for example symptoms such as abdominal/leg pain, thromboembolic events or fever."

Changes in the text: above

What was the shortest follow-up period?

Reply 8: We made a great effort to have as many patients as possible with at least 1 year of follow-up. However in a minimum number of patients, this was not feasible as data of general practitioners was lacking. There was 1 patient with no follow-up at all, 9 patients with <4 weeks and 18 patients with <10 weeks. As presented in the article: The median final follow-up time was 29 months (IQR 22-36); 367 patients had more than 12 months of follow-up.

Changes in the text: line 179: added: In 28 patients the follow-up was shorter than 10 weeks.

- The different surgical techniques are a limitation of the study. Different PLND templates, peritoneal fixation/interposition flaps (only one surgeon used this technique), coagulation, clipping. All this may have an influence on the incidence of lymphoceles and should be discussed accordingly in the limitation section (which does not exist yet).

Reply 9: We thank the reviewer for pointing this out. We have changed the location of the limitation section to the end of the discussion. We have added the above mentioned suggestion.

Changes in the text: line 300 : added: Although variation in surgical technique may have an impact on SLC, no difference between surgeons was found in this study.

- Please provide information of variables of the multivariable analysis in the methods section.

Reply 10: We have added table 3 in which all variables are mentioned.

Changes in the text: line 208 added: “per unit of five”.

- One of the main findings of the study is that BMI is an independent predictor of sLC. This is even stated in the Conclusions. Unfortunately, the multivariate analysis that gave us this result is not presented in a table.

Reply 11: We have added table 3, Multivariable logistic regression on incidence of SLCs (n=401).

Changes in the text: -

- For the same reason, this result should be discussed in more detail. There are at least two other studies in which BMI could be demonstrated as independent predictors in multivariate analyses.

Reply 12: The reviewer is correct; two other studies demonstrated BMI is an independent predictor in MVA. However, literature is inconsistent, since two more studies do not find BMI to be an independent predictor.

Changes in the text: Line 261: added: “We found only BMI as a predictor of SLCs, similar to two recent studies by Sforza et al. and Goßler et al. (17, 18). Interestingly, literature is inconsistent: Capitanio et al. and Gotto et al. in two older studies do not find BMI as a significant predictor of SLCs (14, 16).

- The discussion begins with strengths and limitations of the study. It would be better to describe these separately in another section.

Reply 13: We have changed the location of the strengths and limitations of the study within the discussion section.

Changes in the text: line 293.

- Do the authors draw a conclusion for their clinical practice from their study results?

Reply 14: Yes, definitely. After our study, surgeons are more aware that the complication is more common than previously thought, likely due to centralization of care, and now discuss 7-8% complication rate with patients preoperatively.

Changes in the text: -

Reviewer B

The authors undertook an analysis of a study cohort comprising 404 patients who underwent robot-assisted radical prostatectomy (RARP), including pelvic lymph node dissection (PLND), in relation to the development of symptomatic lymphoceles (sLC). With a median follow-up of 29 months, sLC was observed in 7.4% of patients (n=30). The sole factor demonstrating independent influence on the occurrence of sLC was the patients' Body Mass Index (BMI). From my perspective, these findings do not appear to warrant noteworthy attention, as the study introduces more inquiries than it ultimately addresses.

Several points give rise to concerns that may impede the manuscript's acceptance in a journal with an Impact Factor (IF) exceeding 2:

1. The inclusion in the abstract of a reference to surgeons estimating sLC frequency at 1-2% raises questions about the identity of these surgeons. Surgeons who possess the capability to engage with medical literature are well-aware that sLC frequency ranges between 2 and 10%.

Reply 4: We thank the reviewer for this valuable feedback. With a broad SLC definition (imaging confirmed lymphoceles with symptoms, not only invasively but also conservatively treated), and a longer than usual follow-up we aim to bring novelty. The 1-2% mentioned in our manuscript was based on an older study from another centre in the Netherlands (Van der Poel et al. K Endourol 2012; 26: 1618-1624). In the revised version of our manuscript, we have rephrased this paragraph and specifically excluded the 1-2%.

Changes in the text:

Line 35: ~~At a high volume operating centre, where follow up was decentralised, surgeons assume an incidence of 1-2% which we hypothesize to be an underestimation.~~

Line 50: ~~There was a discrepancy between the incidence we found in this study and the surgeons' expected incidence of SLCs, presumably due to decentralized follow up, suboptimal registration and late symptomatic presentation.~~

line 96: The reported incidence on SLC varies from 0-12%, with recent studies focussing on operating techniques reporting incidences toward the upper end of the spectrum (2, 9-11). Possible explanations for the relatively wide incidence range are different SLC definitions, late presentation or care-setting. ~~As postoperative follow up is performed decentralized after a centralised surgery, we hypothesize that surgeons underestimate the incidence of SLCs after PLND during RARP.~~

Line 103: In this study we investigate the incidence of SLCs in a centralized high-volume operating centre and assess predictive factors and treatment, both conservative and invasive.

Line 304: In this retrospective cohort study we identified an SLC incidence of 7.4%. Many patients presented later than the centralized surgeons' postoperative follow-up. ~~which could in part be explained by its rather late presentation after surgery and decentralised follow up.~~

2. Numerous intriguing variables that could be influential in assessing sLC development were omitted from the study (e.g., ad-1: ligating lymphatic vessels adjacent to the Cloquet lymph node, a practice likely undertaken by one of the surgeons; ad-2: application of monopolar vs. bipolar current for lymphatic vessel coagulation; ad-3: execution of a Peritoneal Interposition Flap (PIF), a technique employed by at least one surgeon, involving "peritoneal fixation"; ad-4: insertion of a drain and duration of drain placement; ad-5: incorporation of hemostatic agents within the lymph node dissection area; ad-6: surgeon-dependent impact; ad-7: duration of surgical procedure as referenced in manuscript citation 11).

Reply 2: The reviewer mentions interesting variables. The surgical technique was not the primary study objective, but is now added in the limitation-section. A significant difference in SLC incidence between surgeons was not found in our study (data not shown). It was impossible to perform a more in depth analysis due to the retrospective nature of the study.

Changes in the text:

line 300 : added: "Although variation in surgical technique may have an impact on SLC, no difference between surgeons was found in this study."

Line 142: "Per-operative drain placement was not performed."

3. The outcome regarding the independent influence of BMI is not novel and has previously been documented in less esteemed journals (e.g., as seen in reference 11 within the manuscript).

Reply 3: The reviewer is correct; two other studies demonstrated BMI is an independent predictor in MVA. However, literature is inconsistent, since two more studies do not find BMI to be an independent predictor.

Changes in the text: Line 261: added: "We found only BMI as a predictor of SLCs, similar to two recent studies by Sforza et al. and Goßler et al. (17, 18). Interestingly, literature is inconsistent: Capitanio et al. and Gotto et al. in two older studies do not find BMI as a significant predictor of SLCs (14, 16).

4. The sLC definition is incomplete, as it fails to account for lymphoceles in close proximity to the bladder, which subsequently induce urgency or exacerbate urinary (in)continence issues.

While Meenderink et al.'s manuscript exhibits sound methodological design, the predetermined criteria were not meticulously devised ex ante, thus preventing the emergence of novel clinical treatment insights from the study's outcomes.

Reply 4: We added the definition of lymphoceles to the Background.

Changes in the text: line 82 added: "lymph fluid-filled collections within the body lacking epithelial lining (6, 7)

Leading in our registration of a lymphocele was its presence on imaging. Imaging was not routinely performed, but only if there was clinical suspicion of an SLC. To sketch some examples of symptoms rousing clinical suspicion of SLC, but not create an exhaustive list, we mentioned some symptoms. We have changed the text to clarify:

Changes in the text:

line 153. Diagnosis of an SLC, ~~supported by symptoms of postoperative abdominal/leg pain, thromboembolic events or fever,~~ was registered if confirmed by ultrasound, CT, or magnetic

resonance imaging. Imaging was not routinely performed, but only if there was clinical suspicion of an SLC due to for example symptoms such as abdominal/leg pain, thromboembolic events or fever.

Reviewer C

I congratulate the authors for this interesting analysis. The manuscript is well-written, the applied methods are sound, and the discussion is balanced. This topic is relevant to readers because lymphoceles are among the most common complications of radical prostatectomy with PLND. The strengths of this study are the long follow-up period and the fact that the patients' general practitioners or referring urologists were contacted for follow-up data.

Reply 1: We thank the reviewer for their appreciation and critical appraisal of the manuscript.

Major issue #1:

The "background" part of the manuscript differs between the abstract and the main manuscript (!?!). In the "Background" (Abstract) you state that: "surgeons assume an incidence of 1-2%". May you elaborate on where these numbers originate (at our institution, we assume a 7-8% rate)?

Reply 2: We thank the reviewer for pointing out this remark. We revised our manuscript and harmonized the abstract and background. The 1-2% mentioned in our manuscript was based on an older study on RARPS from another center in the Netherlands (Van der Poel et al. J Endourol 2012; 26: 1618-1624). In the revised version of our manuscript, we have rephrased this paragraph and specifically excluded the 1-2%.

Changes in the text:

Line 35: ~~At a high volume operating centre, where follow-up was decentralised, surgeons assume an incidence of 1-2% which we hypothesize to be an underestimation.~~

Line 50: ~~There was a discrepancy between the incidence we found in this study and the surgeons' expected incidence of SLCs, presumably due to decentralized follow-up, suboptimal registration and late symptomatic presentation.~~

line 96: The reported incidence on SLC varies from 0-12%, with recent studies focussing on operating techniques reporting incidences toward the upper end of the spectrum (2, 9-11). Possible explanations for the relatively wide incidence range are different SLC definitions, late presentation or care-setting. ~~As postoperative follow-up is performed decentralized after a centralised surgery, we hypothesize that surgeons underestimate the incidence of SLCs after PLND during RARP.~~

Line 103: In this study we investigate the incidence of SLCs in a centralized high-volume operating centre and assess predictive factors and treatment, both conservative and invasive.

Line 304: In this retrospective cohort study we identified an SLC incidence of 7.4%. Many patients presented later than the centralized surgeons' postoperative follow-up. ~~which could in part be explained by its rather late presentation after surgery and decentralised follow-up.~~

Furthermore, many statements are without proper literature citation in the "background"(main manuscript). For instance, the statement: "the effect of salvage PLND in oligo metastatic disease

on delaying hormonal therapy is generally accepted as indirect proof of the therapeutic benefit of PLND." is controversial and requires at least some proper citations. In fact, the therapeutic effect of PLND has not been proven in prostate cancer (two negative RCTs, a negative systematic review quoted by the authors).

However, this is not the focus of your analysis. I would suggest focusing more on the complications of PLND than on the oncological effect. In fact, I would discuss different surgical techniques to reduce lymphocele such as pelvic flaps etc.

Reply 3: We thank the reviewer for this comment.

Changes in the text: line 83 deleted: ~~Discussion remains on the therapeutic benefit and optimal extent of a PLND. The effect of salvage PLND in oligo-metastatic disease on delaying hormonal therapy is generally accepted as indirect proof of the therapeutic benefit of PLND. However, a recent meta-analysis showed no improvement of oncological outcomes with PLND (4, 5).~~

Major issue #2:

Is sonography for screening asymptomatic lymphocele routinely performed at GP/urologists/your center?

Reply 4: This mentioned in the manuscript;

line 129 "Postoperative imaging was not performed routinely." Therefore, asymptomatic lymphocele were incidental findings. We added an extra sentence to clarify:

Changes in the text: Line 155: "Imaging was not routinely performed, but only if there was clinical suspicion of an SLC due to for example symptoms such as abdominal/leg pain, thromboembolic events or fever."

Major issue #3:

Were complications, such as thromboembolic events and edema, only analyzed in patients with SLC? Alternatively, were patients with complications without SLC included? Please clarify this in your manuscript.

Reply 5: Complications such as thromboembolic events and oedema were analysed in all patients; not only in patients with SLC. To clarify, we added an extra sentence.

Changes in the text: line 122: "Complications were assessed in all patients."

Major issue #4:

Please report the results of your uni- and multivariable analyses as a table for clearer understanding. Please specify, which characteristics were included in the multivariable model? Were only characteristics significant in univariable analysis included in the multivariable model? Please describe how the parameters were coded (continuously versus groups). Currently, the multivariable model is not reproducible. There are several concerns regarding the statistics presented herein. In general, please adhere to the recommendations for showing statistics by Assel et al. (Guidelines for Reporting of Statistics for Clinical Research in Urology).

Reply 6: Table 1 shows univariable analyses on patients with and without SLC, including the variables used for multivariable analysis.

We have added table 3 in which the variables, variable coding and results of our multivariable analysis are mentioned. We believe the multivariable model is now reproducible.

As mentioned by Assel et al. under 5.5, we avoid reporting both univariate and multivariable analyses; (so univariable log regr is not reported).

Due to the limited number of events, only pre-determined variables based on literature were selected for the multivariable analysis. As mentioned by Assel et al. under 5.2, we avoided stepwise selection (first determining which variables are statistically significant on univariable analysis).

As mentioned by Assel et al. under 5.4, we rescaled a predictor to obtain interpretable estimates; we used BMI per unit of five for interpretation purposes.

Changes in the text: line 208 added: "per unit of five".

Major issue #5:

In your methods, you nicely describe the differences in surgical techniques between the different surgeons. Was this addressed in the analyses? There is a discussion concerning the use of peritoneal flaps for the reduction of lymphoceles (at least 5 RCTs with different results). In addition, the use of cautery versus clipping of lymph vessels is suspected to influence the lymphocele rates. I strongly suggest addressing this on a surgeon level or discuss it more extensively in the limitations section.

Reply 7: We thank the reviewer for bringing up the very interesting discussion on surgical techniques. The surgical technique was not our primary study objective, but is now added in-text as a possible influence on SLC incidence in the limitations. A significant difference in SLC incidence between surgeons was not found in our study (data not shown). It was impossible to perform a more in depth analysis due to the retrospective nature of the study.

Changes in the text: line 300 : added: Although variation in surgical technique may have an impact on SLC, no difference between surgeons was found in this study.

Major issue #6:

Please provide a proper limitation section for your discussion.

Reply 8: we have created a limitation section at the bottom of the Discussion.

Changes in the text: line 293: The study has some limitations. Selection bias is inherent as this is a retrospective cohort study. Misclassification bias could be present in our study, as it is sometimes unclear whether symptoms should be attributed to a lymphocele. We may have underestimated the incidence since all SLCs had to be confirmed by imaging. Also, standard postoperative follow-up was not specifically targeted at SLCs. Follow-up consisted mainly of oncologic follow-up and monitoring of impotence and urinary incontinence. SLCs were possibly missed as patients could have been treated at another hospital. Although variation in surgical technique may have an impact on SLC, no difference between surgeons was found in this study.

Minor issue #1

The abbreviation "SLC" is not common knowledge or is defined in the abstract, but is used.

Please also explain all nontrivial abbreviations used in the abstract within the abstract.

Reply 9: We thank the reviewer for the remark.

Changes in the text: Line 33: added: a symptomatic lymphocele (SLC)

Minor Issue #2:

For rates, please report the count of the reference cohort. I.e., 30/404 (7.4%) patients with an SLC were identified. Please re-check the numbers, and I am not sure if they always add up because of the missing reference groups.

Reply 10: We have re-checked the numbers and confirmed they add up.

Changes in the text:

Line 195: added: “of 30 SLC”. Line 198: added: (n=374). Line 199: added: “of 30”. Line 219: added: “the 30”

Comment #1:

PSMA-PET imaging is an excellent tool that is insufficient to replace lymph node staging with PLND. It is technically not possible to assess many micrometastases in upfront PET (see Jilg et al. J Nucl Med 2019). The implication is that more research is needed on surgical techniques to reduce SLCs.

Reply 11: The mentioning of PSMA-PET/CT here is meant as an example of how preoperative patient selection tools could be improved in the future.

Soeterik et al. states, “Nevertheless, missed lesions occur in a small percentage of the overall primary prostate cancer patient population and predominantly include small nodal lesions (<5mm). The prognostic impact of missing these small nodal lesions is poorly understood.” The intention of the PSMA-SELECT trial is to assess whether PSMA PET/CT could be of value as a triage tool for ePLND by improving patient selection, and will provide additional insights into the prognostic impact of small nodal lesions in the primary setting

Changes in the text: line 76: deleted: such as a pre-operative PSMA scan.

line 288 added: for example

line 290 added: taking into account possibly missing micro-metastases

Reviewer D

The author performed a retrospective study assessing the incidence, treatments, and risk factors for the development of Lymphoceles following PLND and robotic-assisted radical prostatectomy. The study does not add much to the current knowledge on this topic (i.e. same incidence as in Ploussard’s systematic review) and has several methodological biases which may have affected results. I have the following comments

1) The most important flaw is the difference in how surgery and PLND were done among surgeons. Indeed, peritoneal fixation and treatment of lymphatic vessels (i.e. mono or bipolar coagulation vs. clips) may have different impacts on lymphocele formation. The series should be homogenous.

Reply 1: We thank the reviewer for bringing up the very interesting discussion on surgical techniques.

A significant difference in SLC incidence between surgeons was not found in our study (data not shown). It was impossible to perform a more in depth analysis due to the retrospective, observational nature of the study.

Changes in the text: line 300: added: Although variation in surgical technique may have an impact on SLC, no difference between surgeons was found in this study.

2) Another flaw is related to the fact that some SLC patients were not evaluated by the authors in person but data were just taken from the patient's medical record. This is another bias.

Reply 2: This is indeed a bias in our retrospective study. This is explained in the limitations section in line 294.

Changes in the text: -

3) The third flaw is the low accuracy of their multivariable model which yielded an AUC of only 0.611

Reply 3: The intention of the multivariable model was not to make a highly-predictive model, but rather evaluate variables known from literature. The low AUC means that using these three variables, there is very low accuracy in predicting SLC development. Since this was not the goal, we posit it is not a significant flaw of the study.

Changes in the text: -

4) Abstract. Please, expand SLC when it first appears

Reply 4: We thank the reviewer for the remark.

Changes in the text: Line 33: added: symptomatic lymphoceles (SLC)

5) Results, main text. The authors stated, "In 49 patients, we contacted the general practitioner; in 62 patients the referring urologist was contacted". How were the remaining patients followed up? What was requested from the general practitioners and referring urologist? Just data or patients were re-evaluated in case of suspicious SLC?

Reply 5: The hospital records from all patients were reviewed for complications. If the follow-up was shorter than 1 year, the general practitioner and/or referring urologist were contacted for data on symptoms and last-date of follow-up, the patients were not re-evaluated in person.

Changes in the text: -

6) Results, main text. There is no table for uni and multivariable analysis of predictive factor. This absence does not help to understand the logistic regression model. Yet, decision curve analysis for ROC is also missing

Reply 6: We have added table 3 in which all variables are mentioned. A decision curve analysis is only relevant if the aim of the manuscript is to present a prognostic model. However, this is not the case.

Changes in the text: line 208 added: "per unit of five".

Reviewer E

In the present paper, the authors evaluate the incidence and treatment of lymphoceles after PLND during RARP and determine predictive factors for the development of SLCs
Overall, attention has been paid to the accuracy of the text.

Title: accurate

Abstract: reflects the report

Introduction: clearly states background.

M&M: it is well known that lymphocele formation is affected by surgical approach (trans- vs extra-peritoneal) and technical aspects (extended or limited PLND, drainage placement or no drain at the end of surgery, ligation or coagulation of lymphatic vessels, etc.). Did the authors place a drain in the end of surgery?

Reply 1: We thank the reviewer for their evaluation of our manuscript.

Per-operative drain insertion/ placement was not performed.

Changes in the text: line 143: added: Per-operative drain placement was not performed.

Results: how many lymphoceles were monolateral or bilateral ?

Reply 2: In 6/30 patients the lymphoceles were bilateral, and in 24/30 monolateral.

Changes in the text: -

Discussion: in the end of section, please discuss limitations of the study

Reply 3: we have created a limitation section at the bottom of the Discussion.

Changes in the text: line 293: The study has some limitations. Selection bias is inherent as this is a retrospective cohort study. Misclassification bias could be present in our study, as it is sometimes unclear whether symptoms should be attributed to a lymphocele. We may have underestimated the incidence since all SLCs had to be confirmed by imaging. Also, standard postoperative follow-up was not specifically targeted at SLCs. Follow-up consisted mainly of oncologic follow-up and monitoring of impotence and urinary incontinence. SLCs were possibly missed as patients could have been treated at another hospital. Although variation in surgical technique may have an impact on SLC, no difference between surgeons was found in this study.

Conclusions: clear

Reply 4: We thank the reviewer for their contribution.

Reviewer F

In this manuscript the authors evaluated the incidence, risk factors and treatment of a consecutive series of patients who underwent PLND during RARP. At MVA, only BMI significantly increased the odds of SLC development. Thus, the authors stated that due to the high number of serious complications, the use of PLND needs to be re-evaluated especially considering the rapid paradigm shift towards PSMA scan in the setting of primary staging. Whereas, no impact of number of lymph nodes removed (as continuous variable) was noted at MVA.

Major:

Another important point of discussion is the concept of sentinel lymph node biopsy. Several reports highlighted the safety, reliability and diagnostic accuracy of such a technique in the context of localized PCa undergoing radical treatment. The authors should further discuss this topic in the appropriate section of the manuscript as a novel, tailored approach able to further refine and personalize PLND in such a clinical scenario (doi: 10.3390/diagnostics13152543; doi:

10.1016/j.eururo.2013.11.017; doi: 10.1111/bju.16117; doi: 10.1016/j.eururo.2016.09.007; doi: 10.1016/j.urolonc.2022.08.005; doi: 10.1111/iju.14513; 10.1007/s00345-018-2330-7).

Reply 1: We thank the reviewer for pointing us to this interesting subject.

Changes in the text: line 278 added: "Operative techniques could be improved by the promising sentinel lymph node procedure, and might shift from risk-based to target-based surgery (22)."

Minor:

SLC acronym in the abstract was not declared.

Reply 2: We thank the reviewer for this observation.

Changes in the text: Line 33: added: symptomatic lymphoceles (SLC)

Reviewer G

Jonas J.L. Meenderink et al. in the article titled: "Lymphoceles after pelvic lymph node dissection during robot-assisted radical prostatectomy." performed a retrospective analysis of the complication lymphocele. A very interesting topic, especially since in many cases this complication is marginalized. The observations obtained by the authors are very interesting, especially in the aspect of decentralization of care for patients undergoing surgery and the lack of evaluation of the postoperative course - thus underestimating the number of complications in centers performing RARP with LND.

However, the work requires correction before it is qualified for the next editorial stages.

Comments:

- systematization of numerical data - presentation of % data should be standardized in the text: either digits or written numerals

Reply 1: We thank the reviewer for this comment; we have harmonized it.

Changes in the text:

Line 93: ~~Nil to eight per cent of patients~~

Line 128: 5%

Line 215: 0.614 (95%CI 0.500-0.722).

- Line - 76-79 - sentence - The effect of salvage PLND in oligo metastatic disease on delaying hormonal therapy is generally accepted as indirect proof of the therapeutic benefit of PLND. However, a recent meta-analysis showed no improvement of oncological outcomes with PLND (4, 5). - Completely unrelated to the topic of the study - different indications, different type of surgery and, above all, different % of complications. It should be deleted.

Reply 2: We thank the reviewer for this comment.

Changes in the text: line 83 deleted: ~~Discussion remains on the therapeutic benefit and optimal extent of a PLND. The effect of salvage PLND in oligo metastatic disease on delaying hormonal~~

~~therapy is generally accepted as indirect proof of the therapeutic benefit of PLND. However, a recent meta-analysis showed no improvement of oncological outcomes with PLND (4, 5).~~

- lines 90-103 - the SLC abbreviation should already be expanded in the abstract - the first time it is used (the explanation appears only in the text, line 86)

Reply 3: We thank the reviewer for this observation.

Changes in the text: Line 33: added: symptomatic lymphoceles (SLC)

- line 104 - immeasurable - replace with undetectable

Reply 4: We thank the reviewer for this remark.

Changes in the text: line 118 immeasurable replaced with undetectable

- line 119-12 - Conform the NeuroSAFE procedure, the neurovascular bundles adjacent to the prostate may be spared more frequently if frozen section analysis of surgical margins are negative. - this sentence does not add anything important and is unnecessary

Reply 5: Conform the reviewers comment we deleted this sentence, and kept the part to explain PLND was performed during the frozen section analysis.

Changes in the text: line 137: ~~Conform the NeuroSAFE procedure, the neurovascular bundles adjacent to the prostate may be spared more frequently if frozen section analysis of surgical margins are negative.~~The PLND was performed during the frozen section analysis conform NeuroSAFE procedure (12).