Author’s response to reviews

Title: Retzius-sparing Robot-assisted Laparoscopic Radical Prostatectomy: Functional and Early Oncologic Results in Aggressive and Locally Advanced Prostate Cancer

Authors:
Joanne Nyaboe Nyarangi-Dix (JoanneNyaboe.Nyarangi-Dix@med.uni-heidelberg.de)
Magdalena Görtz (magdalena.goertz@gmail.com; magdalena.goertz@med.uni-heidelberg.de)
Georgi Gradinarov (ge.gradinarov@gmail.com)
Luisa Hofer (luisa.hofer@med.uni-heidelberg.de)
Viktoria Schütz (Viktoria.schuetz@med.uni-heidelberg.de)
Claudia Gasch (claudia.gasch@med.uni-heidelberg.de)
Jan Philipp Radtke (JanPhilipp.Radtke@med.uni-heidelberg.de)
Markus Hohenfellner (markus.hohenfellner@med.uni-heidelberg.de)

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Magdalena Görtz, MD
Im Neuenheimer Feld 110
69120 Heidelberg
Germany
magdalena.goertz@med.uni-heidelberg.de
Tel.: +49 6221 568820
Fax: +49 6221 565188

Tillie Cryer
Editor
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Dear Ms. Cryer:

Thank you very much for the consideration of our manuscript “Retzius-sparing Robot-assisted Laparoscopic Radical Prostatectomy: Functional and Oncologic Results in Aggressive and Locally Advanced Prostate Cancer”, reference BURO-D-19-00077, for publication in BMC Urology. Thank you for the reviewer’s comments and for giving us the opportunity to improve our manuscript accordingly. Please find below a point by point response to the suggestions. The manuscript underwent thorough revision.

Yours sincerely,

Magdalena Görtz

We address the comments of the reviewers as following:

Reviewer reports:

Geoff Coughlin (Reviewer 1): Please overwrite this text when adding your comments to the authors.

Christopher Eden, MBBS MS FRCS(Urol) (Reviewer 2): The authors present a small (n=50) retrospective single-centre series of men with high-risk prostate cancer having robot-assisted radical prostatectomy (RARP) using a Retzius-sparing (RS) technique with 12 months' follow-up. Continence levels at 3 and 12 months were high at 82% and 98% and positive surgical margin (42%) and potency rates after uni- or bi-lateral nerve preservation were good at 42%.

Methods
The RS-RARP technique described by Galfano utilized 2 (not 4) sutures to retract the superior aspect of the peritoneotomy.


What were exclusion criteria for RS-RARP? Were patients with anterior tumours included and if so with what results?

Since adapting Retzius-sparing prostatectomy in our centre, all men viable for RARP were operated in this manner, regardless of preoperative oncological characteristics (Discussion section, page 9, lines
There were no exclusion criteria for rsRARP. Retrospectively, we identified 11 patients with an anterior index tumor in imaging. 8 of 11 (73%) patients with anterior tumors had pT3-disease and 5 of 11 (45%) had PSM. As suggested, we included this information in Results section, pages 7-8, lines 162-163.

Douglas Skarecky (Reviewer 3): The authors present their early descriptive experience of rsRARP outcomes in high risk CaP patients. In early reporting of RARP single pad continence and any successful intercourse was considered successful, but for current RARP patients rely on more sophisticated results. The authors have gathered but not reported pre and postop IPSS and IIEF-5 scores and unfortunately only chose to report minimal definitions of continence and sexual function, and the paper is not acceptable as it is presented.

Liss et al (J Urology 183(4), 2010) has shown that men with one or security pad continence are more similar to multiple pad users than men declared as pad free. To be more transparent the abstract should present continence data with the restrictive 'pad free' rates in addition to the 'single pad' rates. The KM curve shows the pad free rates at ~38% at 1M, ~50% at 3M and ~75% at one year, which are less than or equal to existing to current RARP rates, please comment in the discussion.

Thank you very much for your remark and the reference. As suggested, we included the continence data with the "pad free" rates in addition to the "single pad" rates in the abstract of the revised manuscript (Abstract, page 2, lines 40-41). Studies of patients with high risk or locally advanced prostate cancer show heterogeneous continence outcomes after RARP. The necessity of extended and wide resection in locally advanced prostate cancer can result in worse urinary function compared to localized cancer (Saika T, Miura N, Fukumoto T, Yanagihara Y, Miyauchi Y, Kikugawa T. Role of robot-assisted radical prostatectomy in locally advanced prostate cancer. Int J Urol. 2018;25(1):30-5.). Gandaglia et al. found a 1-year urinary continence recovery rate of 64% after conventional RARP in locally advanced cancer (defined as the use of no pad) (Gandaglia G, De Lorenzis E, Novara G, Fossati N, De Groote R, Dovey Z, et al. Robot-assisted Radical Prostatectomy and Extended Pelvic Lymph Node Dissection in Patients with Locally-advanced Prostate Cancer. Eur Urol. 017;71(2):249-56.). We included this information in the Discussion section, page 11, lines 245-247 and 250-252).

IPSS scores were gathered but omitted. Please present these pre/post scores by individual category as they could complement the continence rates, and explicitly show the expected urinary quality of life (QOL) outcomes of rsRARP men.

The objective of our study is to demonstrate the feasibility of rsRARP in a purely aggressive prostate cancer collective in terms of a proof of concept. Unfortunately, we didn’t gather the postoperative IPSS scores. We clarified it in the Methods section, page 6, line 120 of the revised manuscript. We are unable to reliably add the postoperative IPSS scores of our cohort retrospectively. Previous literature about rsRARP defined the postoperative quality of micturition similarly to our study, according to the pad use and not to IPSS scores (e.g. Galfano A, Di Trapani D, Sozzi F, Strada E, Petralia G, Bramerio M, et al. Beyond the learning curve of the Retzius-sparing approach for robot-assisted laparoscopic radical prostatectomy: oncologic and functional results of the first 200 patients with &gt;= 1 year of follow-up. Eur Urol. 2013;64(6):974-80.)

The shortcomings of time to sexual function, small sample size, and short term follow up are insufficient support for the potency findings of "surprisingly positive" and "very good results" stated in the abstract and paper conclusions and should be revised.
Thank you for your remark. As suggested, we revised the manuscript accordingly (Abstract, page 3, lines 53-54 and Conclusions section, pages 13-14, lines 311-313).

With pre and post IIEF-5 scores available for all 50 men, patients and physicians require more detailed information. It is unclear from the time to intercourse stated result, if potency is based on a single act of sexual intercourse or more consistent results. If potency is based on a single act, this is hardly satisfactory to men, in fact very frustrating and a poor indicator of RARP success.

Our apologies for the confusion. All seven patients who had their first sexual intercourse within the first year of surgery reported about stable and consistent results. We included this information in the Results section, page 8, line 185.

To clarify the success of rsRARP, please provide a new table that separates all the preop men by either IIEF-5 scores &gt;17 or &gt;17. Better yet would be 0-15 (impotent), 16-21 (ED), and 22+ (potent) and then again how each group fared at 12 months (3x3 table). This would give us a clear picture of sexual function for all the 50 rsRARP men.

Thank you very much for your comment. We fully agree with your statement that a comparison of the preoperative and postoperative IIEF-5 scores gives a clearer picture of the sexual function recovery in our cohort. Accordingly, we included this information in supplementary material 2A.

Likewise, time to sexual intercourse is a novel finding but very difficult to compare with existing RARP literature. It is unclear whether men are or are not fully potent after rsRARP, thus the paper needs to fully describe whether the IIEF frequency (Q3) and satisfaction scores (Q5) for these men average 1/2 or 4/5, very important scales for men considering rsRARP.

Thank you very much for your remark. For the 7 postoperatively potent patients, the median IIEF frequency score (Q3) to maintain the erection during sexual intercourse was 4 (IQR: 3-4) and the median IIEF satisfaction score (Q5) was 4 (IQR: 4-5). As suggested, we included this information in the revised manuscript in the Results section, page 9, lines 188-190.

The 22% of men with ADT will likely be impotent from poor libido, but from your results, it is unknown if these men were impotent or potent preop. Of the 29 men had IIEF &gt;17, how many of these men were fully potent, ED, impotent or ADT at one year? Also it must be discussed if this study truly has enough men at one year to make any meaningful conclusion for potency after rsRARP?

Thank you for your remark. As suggested we have included a table with the relevant information as supplementary material 2B.

Furthermore, we have included the following statement to the limitations of our manuscript: „Lastly, the promising first results of sexual function recovery after rsRARP in a purely aggressive PCa-collective need to be confirmed in larger cohorts and over a longer period of time.“ (Discussion section, page 13, lines 302-304).

The authors stated all men at their institution received rsRARP, whether low or high risk. Please add a paragraph giving the results for the low risk men in the same time period.

The objective of our study is to demonstrate the feasibility of rsRARP in a purely aggressive prostate cancer collective. Since the Bocciardi group described their technique of rsRARP, various subsequent
studies reported excellent functional and oncological outcomes for low- and intermediate-risk prostate cancer (Dalela D, Jeong W, Prasad MA, Sood A, Abdollah F, Diaz M, et al. A Pragmatic Randomized Controlled Trial Examining the Impact of the Retzius-sparing Approach on Early Urinary Continence Recovery After Robot-assisted Radical Prostatectomy. Eur Urol. 2017;72(5):677-85.). Therefore, we didn’t gather the results for the corresponding low risk group in the same time period, unfortunately. We are unable to reliably add this information in retrospect. In light of the results of the current study, we recently initiated a prospective randomized clinical trial at our institution that compares the outcomes of conventional and rsRARP in low-, intermediate and high-risk prostate cancer. However, these results are pending and weren’t collected in the same time period as our high-risk prostate cancer collective.

Minor comments

How many pads was the one man at 12months using? Single or multiple?

Thank you for your remark. The one man who used >1 safety pad per day used two pads per day. We included this information in the Results section, page 8, line 177.

Please add Phukan et al (World J Urology May 2019) to the references.

Thank you very much for suggesting this reference. We included the review as a reference in our revised manuscript (Discussion section, page 9, lines 194-196).

Please note a recent editorial by Stonier et al supports the need for your paper (BJU 2019 123; 5-10)

Thank you for this relevant editorial. We are referring to Stonier et al. in the Background section, page 4, lines 79-81 of the revised manuscript.