Author's response to reviews

**Title:** Impact of intraoperative fluid administration on outcome in patients undergoing robotic-assisted laparoscopic prostatectomy - a retrospective analysis

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**Version:** 2 **Date:** 18 March 2014

**Author's response to reviews:** see over
Dear Editor,

Enclosed please find the revised version of our manuscript entitled:

**Impact of intraoperative fluid administration on complications and length of hospitalisation in patients undergoing robotic-assisted laparoscopic prostatectomy – a retrospective analysis**

which is being re-submitted for publication in *BMC Anesthesiology* by Tobias Piegeler, Pamela Dreessen, Sereina Graber, Sarah R. Haile, Daniel Max Schmid, and Beatrice Beck-Schimmer.

Please find attached our revised manuscript as well as our response to the Reviewers’ comments, which we very much appreciated and have revised our manuscript accordingly.

This material is original and has not been submitted for publication elsewhere. All authors have read the revised manuscript, attest to the validity and legitimacy of the data and its interpretation, and agree to its re-submission to *BMC Anesthesiology*. All authors declare they have no competing interests.

We hope that this manuscript will now be suitable for publication in your journal.

Sincerely,

Tobias Piegeler, MD
Response to Reviewers’ comments

Reviewer #1

Major
1. Surgeon experience - the authors used the initial 182 cases from initial series from 2005-2008. As they mention, therefore, this was during the beginning of the surgeons learning curve, and surgeon experience is a well known determinant of outcomes following RALP. Why do the authors not use a later series of subjects to minimize the learning curve effect?
2. Along these lines, the authors mention that this included the cases of multiple surgeons. Again, surgeon experience and inter-surgeon heterogeneity of technique can affect outcomes. Are the authors able to account of each surgeon to see if one had more complications than the others?

We would like to thank the reviewer for these two comments. It was our intention to analyze these almost 200 initial cases of RALP at our institution as our anesthesiologists had no experience with this technique and there was no protocol available concerning intraoperative fluid resuscitation to be followed. We thought it would be interesting to see whether non-standardized intraoperative fluid management had an impact on postoperative outcome. At the beginning, when DaVinci was introduced as a new technique in our hospital, only a dedicated, well-trained and skilled team of 4 surgeons was involved in this complex surgery. Most often at least 2 of them were in the OR for one single patient. Therefore, we can guarantee that the factor ‘surgeon’ was not more important than in other trials with involvement of surgical skills. Additionally, we think that in academic operative medicine, with an according educational character, there are always less experienced surgeons present who have to learn a new procedure. Therefore, postponing the beginning of the study would not solve this problem.

Analyzing all complications it became clear and obvious that not a single surgeon was identified to be superior to another.

3. Fluids and impact on OR time: as the authors mention, the median amount of fluids used is very high. We routinely keep fluids less than 2000mL during a case in order to prevent urine leakage into the operative field. I would be curious to see if total amount of fluid used intraoperative affected operative time at all due to this limitation of exposure.

This is another valuable point. There is indeed an effect of the amount of fluid applied on the duration of the surgery, also if additionally corrected for the individual patient’s BMI. This was the main reason why we initially decided to normalize the amount of fluid applied not only to the patient’s BMI but also to the duration of the surgery (ml fluid/unit BMI*minute operation duration).
4. No correlation between blood loss and leak, but what about anastomotic stricture? This should be an endpoint that is looked at. EBL is known to be a risk factor for postoperative anastomotic stricture rate, and I would be curious to see if fluid utilization also has an impact. Do the authors have this information?

*Unfortunately, we did not follow-up on our patients long enough to record the incidence of anastomotic stricture, as this complication usually starts to become evident at 6 months after the surgery at the earliest. Therefore, we do not have this information right now and are not able to draw any conclusions concerning the impact of intraoperative fluid management on the incidence of this particular complication.*

**Minor**

5. Did the older men getting more colloid have higher EBL? This may have lead to higher complications rather than the colloid itself.

*We thank the reviewer for this interesting question. In accordance with the reviewer’s suggestions we performed an additional analysis showing that there was no significant difference in estimated blood loss between the older men (70-80 years old) and the group of patients less than 70 years old. We have added a corresponding text in our manuscript as well (page 12, last paragraph).*

**Discretionary**


*In our institution the vesico-urethral urine leak is diagnosed via cystography on postoperative day (POD) 5. We have added this information in the Results section (page 10, paragraph 2).*

7. There is a much longer length of stay than we are used to seeing in the US and other countries. Is this the norm in the authors native countries? Do they stay in the hospital until the catheter is removed?

*In our institution the patients were hospitalized 1 day prior to surgery. The cystography takes place on POD 5. In case there was no leak, the catheter was removed on POD 7 and the patients stayed for one more day (until POD 8) in order to monitor them once more and also for pelvic floor exercise initiation and instructions.*

8. I would recommend not using the term "neo-urethra" as the authors do. The urethra is the native urethra and not reconstructed to become a "neo-urethra",
therefore this is an inaccurate term. Simply using "urethra" would suffice.

*We have changed the term in accordance with the reviewer’s suggestion throughout the manuscript.*

**Reviewer #2**

1. Need to show the operative parameters? How many surgeons, Operation time, prostate size, the difficulty of operation (previous TURP?)

   *As requested, we have added the duration of surgery as well as the prostate weight to Table 1. Unfortunately, we are unable to report or grade the difficulty of the surgery as it has not been assessed whether the patients has had a TURP before the RALP. However, of course every patient did have prostate biopsies prior to RALP. Additionally, we report that there were 4 different surgeons operating on the patients that were analyzed for this study (2 with major contribution). We have added this number to the Materials & Methods section (page 7, paragraph 1).*

2. The length of hospitalization is related to operation time and anesthesia time?

   *We performed an additional analysis evaluating a possible effect of the duration of surgery on the length of hospitalization as requested by the reviewer. However, there was no significant effect of the duration of surgery on the length of hospitalization (estimate 0.0002246, standard error 0.0003470, p-value 0.518). As this analysis does not provide any gain in knowledge, we therefore decided to not include this data in our manuscript. Of course we will be happy to provide the exact calculations of our statistical software to the reviewer, if requested.*

3. More blood loss will administer colloid, and then more complication? Colloid is the etiology of length of hospitalization? The real etiology is blood loss.

   *We have already performed an analysis examining the influence of intraoperative blood loss on the length of hospitalization. On page 12 of our manuscript we report the results of this analysis: Apparently there was no correlation between blood loss and the length of hospitalization.*

4. The old age is more confounding factor, e.g. ASA score, more co-morbidity. Anesthesiologist will prescribe colloid. It will prolong length of hospitalization?

   *Age itself did not specifically prolong the length of hospitalization. However, as reflected by our results, there is a clear effect of colloid administration on the length of hospitalization in the patients 70-80 years old. There is no evidence in our analysis that ASA score or co-morbidities lead to more colloid*
5. Initial RALP 200 case is need to learning for surgeons and anesthesiologists. Though, the study have delicate bio-statistics analysis. After surgical experience and anesthesia become stable, follow anesthesia protocol, the study will convince readers. The study didn’t mention anesthesia protocol?

As mentioned on page 7, paragraph 4 of our manuscript, there was no specific anesthesia/fluid management protocol that had to be followed by the anesthesiologist in charge. Concerning the valid comment regarding the surgical learning curve please see our response to comments 1. and 2. by Reviewer #1.

6. The principle of fluid administration during RALP in our hospital is 2.5 ml/kg/hr, the median fluid is 600ml/ per procedure (RALP). The anesthesia in this study is not standardization and give too many fluid?

The goal of this study was to evaluate the first 200 cases of RALP in our institution in order to establish a protocol for fluid management during this particular procedure. There was no specific fluid management protocol suggested at the time of the analyzed cases.