Author’s response to reviews

Title: Prediction of postoperative pain after radical prostatectomy

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Version: 2 Date: 16 October 2008

Author’s response to reviews: see over
Please find enclosed a revised version of our manuscript with the title “Prediction of postoperative pain after radical prostatectomy”. We have with great interest taken part of the valuable comments made by the referees and revised our manuscript accordingly regarding most items (see below).

**Reviewer David R Urbach**

**Reviewers report**

1. The second purpose of the study has been further explained. See page 5, paragraph 2, sentence 2 “The influence of previous pain score (Visual Analogue Scale, VAS-value) on the next-coming pain scores has not earlier been studied in this group of patients i.e. if patients who are in pain directly after surgery continue to be in pain during the postoperative recovery.”

2. The time line is now described in the Methods section, first sentence. “The study was a prospective, explorative study conducted from January 2003 to June 2004.” The Statistical analysis on page 9 is now better described “Pitman’s test is a non-parametric test not based on ranks but on the original values. By use of logistic regression analysis we estimated the probability that VAS at one occasion would exceed 30mm or 70mm and the result is presented by graphs calculated from the beta coefficients. The cut-off 30mm was chosen because that is a limit for treatment.”

3. Here the reviewer had no remarks.

4. Of course it would be possible to give a traditional table with OR and 95% confidence intervals. However, in this case a figure giving the probability of VAS larger than 30 or 70 is much more informative. It is not only the OR and the corresponding beta coefficient, which is of importance for the probability, but also the constant in the logistic model. The OR tells us how the odds are increased by an increase of 1 unit of
the VAS scale. The constant of the model, which usually is not shown, is also of importance in this case, because that quantity affects the level of the probability.

Below OR is given corresponding to the first one of the figures of the panel (Figure 1).

**Probability that VAS day 1 > 30**

<table>
<thead>
<tr>
<th>Variable</th>
<th>β</th>
<th>SE</th>
<th>p-value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>-0.5734</td>
<td>0.4707</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Min(VAS 4 hours, 20)</td>
<td>0.0299</td>
<td>0.0403</td>
<td>0.4582</td>
<td>1.03 (0.95 – 1.12)</td>
</tr>
<tr>
<td>Max(VAS 4 hours – 20, 0)</td>
<td>0.1169</td>
<td>0.0652</td>
<td>0.0730</td>
<td>1.12 (0.99 – 1.28)</td>
</tr>
</tbody>
</table>

The table above tells the reader much less than the first figure of the panel.

The finding that preoperative anxiety tended to correlate with postoperative pain has been removed from the text.

5. Nurses’ role in pain management is discussed on page 15. We have also added the following paragraph in the Background section (page 4 and 5) “Nurses are in a unique position to supervise and assist patients in pain and in the treatment thereof, considering the extensive time nurses spend with the patients when compared with other health-team members (Nash et al., 1999). Nursing pain management involves a number of activities; assessing pain and deciding whether to administer analgesics, selecting one of different analgesics and choosing the route of administration. Nurses are also responsible for monitoring the effect of medication which is prescribed and administered in a variety of ways, including PRN (pro re nata, as needed/requested), EDA and ITA (Manias, 2003)”.

6. We have added a headline “Limitations” (page 16) where we discuss the issues that are pointed out by the reviewer.

7. Here the reviewer had no remarks.
8. Here the reviewer had no remarks.

9. The stylistic issues have been corrected. We have made the changes regarding the VAS as an acronym both in abstract and background as follows; Visual Analogue Scale (VAS).

**Discretionary Revisions**

1. The link between nursing and patients’ pain is discussed on page 15, section 2.

2. **Epidural analgesia** (EDA) and **intrathecal analgesia** (ITA) are two different types of spinal analgesia.

3. The last paragraph on page 10 (results related to perceived control, anxiety and depression) has been revised. Hopefully the text is now more logic.

4. Mean PACU time was 14±7 hours with a range of 3-46 hours. Many patients stayed overnight in the PACU and patients with insufficient pain relief had the longest stay.

**Minor Essential Revisions**

1. All references to tables are moved to the “Result” section

2. Only four patients reported some kind of pain before surgery as described under the heading “Pain expectations and pain experiences”, page 9, last sentence. Therefore the correlation between pre- and postoperative pain was not analyzed.

3. The references are now correct

4. We used a piecewise linear function of VAS with a possible breakpoint at VAS=20, see the table above.

5. From a treatment perspective the limit 30 is important (patients above that limit should be treated in accordance to a general policy). That is a reason for considering that cut-off point and that is also the reason why it is important to predict those above that limit, i.e. to predict those who need treatment. A correlation coefficient between a
predictor and a later VAS would not reflect the proportion of patients who will need
treatment depending on a previous value of VAS.

Major Compulsory Revisions

1. Statistical methods are now extended (see page 9).
2. See above
3. The finding that preoperative anxiety tended to correlate with postoperative pain has been removed.
4. Baseline pain scores were 0 except for four patients and therefore we did not use this factor in the univariate analysis. The findings of the correlation between pain at 4h, day 1 and day 2 is important because it seems like patient in pain at 4 hours continue to be in pain and should be treated in the immediate postoperative phase.
5. From a treatment perspective we want to predict whether the patient needs treatment in the next future, so that we, in the best case, can give the treatment before the pain has increased above 30 on the VAS scale. For that purpose we do not need to make a prediction at baseline or by use of the baseline values. We need to make a prediction with a time horizon of a few hours only to get the opportunity to treat the patient.
6. On page 11, last paragraph we describe that in the regression model, the significant variables from the univariate analysis, were included.
7. The patients were not assigned to different pain treatment methods depending on patient factors. As described on page 8 under the heading “Procedure”, sub-heading “Pain treatment routines”, initially EDA was the routine treatment for postoperative pain in these RP patients. About a year after the beginning of the study, and after evaluating EDA as an ineffective method for pain treatment in this group of patients,
the method for postoperative analgesia was shifted to ITA. Study patients who were
deemed unsuitable for either EDA or ITA, received systemic opioids for pain relief.

Anders Odén, professor in biostatistics at Chalmers University of Technology, Gothenburg,
Sweden, has commented the statistical questions.

**Reviewer Robert Slappendel**

**Reviewers report**

We have transformed table 3 to a figure (see below). However we leave to the reviewer/editor
to decide whether these data should be presented as a figure or a table. If the figure is chosen
the numbering of the tables and figures must be changed in the text.

![Figure 1. Differences among pain treatment methods with regard to “worst pain” scores](image-url)