

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Impact of weekday of surgery on application of enhanced recovery pathway – a retrospective cohort study
<b>AUTHORS</b>	ROMAIN, Benoit; GRASS, Fabian; ADDOR, Valerie; DEMARTINES, Nicolas; HUBNER, Martin

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Nader Francis Yeovil District Hospital NHS Foundation Trust UK
<b>REVIEW RETURNED</b>	05-Feb-2016

<b>GENERAL COMMENTS</b>	<p>I reviewed with interest the manuscript by ROMAIN et al comparing enhanced recovery after surgery (ERAS) protocol compliance and clinical outcomes on the weekday of surgery.</p> <p>The manuscript addresses an important and topical issue which is related to the level of service provision over the weekend and the impact of this on the ERAS compliance and outcome.</p> <p>There are however 2 main issues that require addressing:</p> <p>First, there seems to be a confusion across the manuscript about if there was a difference on ERAS compliance between the two groups or not . On one hand, the authors stated that there was significant difference between the total compliance to ERAS protocol was 78% for the early group and 76% for the late group (p=0.009) but not when analysed by the different perioperative periods (pre-, intra- and post-operative). The authors refer to the comparison between the individual elements (pre, intra and postoperative) of ERAS as “equal” but the total of them was significantly different. How could this be possible? More likely the sample size of each subgroup was too small to show any significant difference (type II error) but when they were combined together, they showed a statistical difference. The same could apply to many other items of the comparison between the two groups such as the percentage of open surgery was 32% in the late group compared to only 23% in the early group and, although these were not statistically significant, but may have been be if the sample was bigger.</p> <p>The main issue of the manuscript however is related to the take home message and the educational value of the study which are not very clear in this manuscript. First the authors need to demonstrate the level of weekend ERAS service by describing the structure of the care (nursing, doctors and other MDT members) in their institution, as they refer to “the high staffing level compared to other countries”. This may inform the reader of what is needed in order to achieve high level of ERAS care over the weekend. Then the authors could use their results (or at least some of it) to validate their ERAS service provision over the weekends.</p>
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<b>REVIEWER</b>	Henrik Kehlet Rigshospitalet Copenhagen University Hospital, Denmark
	Only academic conflicts of interest
<b>REVIEW RETURNED</b>	05-Apr-2016

<b>GENERAL COMMENTS</b>	<p>The aim of this study is interesting, since studies from other elective procedures like hip and knee arthroplasty also have suggested longer stay when operations were performed later in the week (Husted H, Holm G, Jacobsen S. Predictors of length of stay and patient satisfaction after hip and knee replacement surgery: fast-track experience in 712 patients. <i>Acta Orthop</i> 2008;79:168-73. + Rathi P, Coleman S, Durbin-Johnson B, Giordani M, Pereira G, Di Cesare PE. Effect of day of the week of primary total hip arthroplasty on length of stay at a university-based teaching medical center. <i>Am J Orthop</i> 2014;43:E299-E303).</p> <p>However, the main problem with this study is the discrepancy between the title “enhanced recovery” and what they are actually doing. Thus, the overall compliance is repeatedly mentioned to be around 77 %, but this is mostly due to some simple and not really clinical relevant preoperative factors mentioned in figure 2, while the really important enhanced recovery factors are the postoperative factors and where the compliance was much lower. Consequently, the study is not a fully implemented enhanced recovery program limiting interpretation and the specific role of “day of operation”. Thus, the study may rather reflect traditions in the department in question. Thus, why was termination of urinary drainage according to protocol only performed in 60 % of patients? Why only 20 % of cases receiving postoperative epidural analgesia which at least in open cases have shown important recovery effects? Importantly, although LOS is reported, we don’t know why the patients were in hospital? Even more important, it is mentioned that major complications were not different but there is no details or discussion on these complications or the pathogenesis of major complications of which according to the Dindo-Clavien classification some in no way are related to enhanced recovery per se, but rather to pure “surgical” factors.</p> <p>Summarizing, although of potential interest, there are several methodological problems that hinder sufficient interpretation. The question raised need to be studied in a fully-implemented enhanced recovery program (the 5 key important elements compared to many of the remaining recommended ERAS factors that are less relevant for recovery). Finally, regarding complications the study is underpowered.</p>
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<b>REVIEWER</b>	Marielle M.E. Coolsen Maastricht University Hospital
<b>REVIEW RETURNED</b>	11-Apr-2016

<b>GENERAL COMMENTS</b>	<p>The authors present a retrospective analysis of a cohort study of consecutive patients undergoing elective colorectal surgery in an ERAS programme and compare compliance and clinical outcomes of patients that were operated early in the week (Monday/Tuesday) with patients that were operated on Thursday and Friday.</p> <p>The authors conclude that clinical outcomes as well as overall ERAS</p>
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	<p>compliance was similar in both groups and that an ERAS programme also appears to work during the weekend.</p> <p>This is an interesting study with a good objective and hypothesis, taking into account previous articles that show worse outcomes for patients undergoing elective surgery before the weekend. Overall, it is well-written, methods and statistical analysis are valid and the discussion is brief and to-the-point.</p> <p>I have some minor comments:</p> <ol style="list-style-type: none"> <li>1. This study shows better outcome than hypothesized and the authors and caregivers in the Lausanne University Hospital are to be complemented for that. However, the major drawback of this study may be that results cannot be reproduced in hospitals where ERAS has not been fully implemented and practiced by each caregiver or in hospitals where staff/services are not as abundantly present and available during the weekend days. Although the authors have already highlighted this in the discussion, in my opinion, it should be stated more clearly in the conclusion of the abstract as well.</li> <li>2. Please provide additional information in table 1: specify the kind of surgical procedures performed. So, what is the number of rectal and colonic resections and the ratio in both groups?</li> <li>3. The authors state that ERAS is applied in accordance with the published ERAS guidelines for colonic and rectal surgery. Although a table in reference 15 probably explains a bit, Figure 1 is unclear to me and raises some questions:             <ul style="list-style-type: none"> <li>- It seems that 95% of patients in both groups have received oral bowel preparation. ERAS guidelines state that oral bowel preparation should be avoided in colonic surgery. So does this mean 95% of the procedures were rectal resections? Or did patients undergoing colonic resections also receive oral bowel preparation?</li> <li>- It looks like 95% of patients in both groups received a nasogastric tube postoperatively. I assume this should be NO nasogastric tube?</li> <li>- ERAS guidelines state that resection site drainage should be avoided in colonic surgery and only be carried out on indication in rectal surgery. Did almost 80% in both groups receive drains?</li> <li>- On what day was urinary drainage/IV fluid infusion terminated in both groups?</li> <li>- "Energy intake on day of surgery postoperative". Is that &gt;600 kcal a day?</li> <li>- Mobilisation at POD..., is that more than 6 hours a day?</li> </ul> </li> <li>4. Line 51: "did not observed" should be "did not observe".</li> </ol>
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**VERSION 1 – AUTHOR RESPONSE**

Reviewer 1: Nader Francis

There are however 2 main issues that require addressing:

First, there seems to be a confusion across the manuscript about if there was a difference on ERAS

compliance between the two groups or not. On one hand, the authors stated that there was significant difference between the total compliance to ERAS protocol was 78% for the early group and 76% for the late group ( $p=0.009$ ) but not when analysed by the different perioperative periods (pre-, intra- and post-operative). The authors refer to the comparison between the individual elements (pre, intra and postoperative) of ERAS as “equal” but the total of them was significantly different. How could this be possible? More likely the sample size of each subgroup was too small to show any significant difference (type II error) but when they were combined together, they showed a statistical difference. The same could apply to many other items of the comparison between the two groups such as the percentage of open surgery was 32% in the late group compared to only 23% in the early group and, although these were not statistically significant, but may have been be if the sample was bigger.

v We agree with Prof. Francis that this part of the manuscript can create confusion and we seize this opportunity to clarify our message. Total compliance with the protocol was 78 vs. 76% for the two comparative groups. This small difference was indeed statistically significant but not of clinical relevance as also shown by the comparable outcomes. Subtle differences exist between the two comparative groups as pointed out by Prof. Francis. It is possible that some of these differences would become significant when including more patients (lower likelihood for type II error). And yet again, it remains to be demonstrated that these rather small differences are really clinically relevant. These important points were addressed in more detail in the discussion.

The main issue of the manuscript however is related to the take home message and the educational value of the study which are not very clear in this manuscript. First the authors need to demonstrate the level of weekend ERAS service by describing the structure of the care (nursing, doctors and other MDT members) in their institution, as they refer to “the high staffing level compared to other countries”. This may inform the reader of what is needed in order to achieve high level of ERAS care over the weekend. Then the authors could use their results (or at least some of it) to validate their ERAS service provision over the weekends.

v Structure of care and staffing differs widely from country to country and we inserted a description of the “Swiss situation” in the methods section as requested. The discussion was adapted accordingly as well sharpening the importance of standardized pathways especially in case of restricted resources (on weekends but also in general).

Reviewer 2: Henrik Kehlet

The aim of this study is interesting, since studies from other elective procedures like hip and knee arthroplasty also have suggested longer stay when operations were performed later in the week (Husted H, Holm G, Jacobsen S. Predictors of length of stay and patient satisfaction after hip and knee replacement surgery: fast-track experience in 712 patients. *Acta Orthop* 2008;79:168-73. + Rathi P, Coleman S, Durbin-Johnson B, Giordani M, Pereira G, Di Cesare PE. Effect of day of the week of primary total hip arthroplasty on length of stay at a university-based teaching medical center. *Am J Orthop* 2014;43:E299-E303).

v We thank Prof. Kehlet for his encouraging comments and suggested references. Although coming from a different field of surgery we agree that they fit well into the discussion that was amended.

However, the main problem with this study is the discrepancy between the title “enhanced recovery” and what they are actually doing. Thus, the overall compliance is repeatedly mentioned to be around 77 %, but this is mostly due to some simple and not really clinical relevant preoperative factors mentioned in figure 2, while the really important enhanced recovery factors are the postoperative factors and where the compliance was much lower. Consequently, the study is not a fully implemented enhanced recovery program limiting interpretation and the specific role of “day of operation”.

v Compliance with the intended protocol is key of success as nicely shown by Gustafsson (ERAS

Compliance Group. The Impact of Enhanced Recovery Protocol Compliance on Elective Colorectal Cancer Resection: Results from an International Registry. *Ann Surg.* 2015 Jun; 261: 1153-9; and Gustafsson UO, Hausel J, Thorell A, et al. Adherence to the enhanced recovery after surgery protocol and outcomes after colorectal cancer surgery. *Arch Surg.* 2011; 146:571-7). Compliance with postoperative care items is indeed much more challenging as it was shown in our study but also by others (Maessen J, Dejong CH, Hausel J, Nygren J, Lassen K, Andersen J, Kessels AG, Revhaug A, Kehlet H, Ljungqvist O, Fearon KC, von Meyenfeldt MF. A protocol is not enough to implement an enhanced recovery programme for colorectal resection. *Br J Surg.* 2007; 94: 224-31). Although we strive for optimal results as achieved by Prof. Kehlet and his team we are not quite yet there! However, we provide honest reporting of outcomes and compliance which is frequently not even reported in studies on enhanced recovery or fast track. Furthermore, we compare favorably with other ERAS centers (Gustafsson UO, Hausel J, Thorell A, et al. Adherence to the enhanced recovery after surgery protocol and outcomes after colorectal cancer surgery. *Arch Surg.* 2011; 146:571-7; Maessen J, Dejong CH, Hausel J, Nygren J, Lassen K, Andersen J, Kessels AG, Revhaug A, Kehlet H, Ljungqvist O, Fearon KC, von Meyenfeldt MF. A protocol is not enough to implement an enhanced recovery programme for colorectal resection. *Br J Surg.* 2007;94: 224-31; and Roulin D, Donadini A, Gander S, Griesser AC, Blanc C, Hübner M, Schäfer M, Demartines N. Cost-effectiveness of the implementation of an enhanced recovery protocol for colorectal surgery. *Br J Surg.* 2013; 100: 1108-14).

Thus, why was termination of urinary drainage according to protocol only performed in 60 % of patients?

v The study cohort included 19.4 % of rectal resections, where urinary drainage was removed on postoperative day 3 or 4 in line with practice guidelines (Lassen K, Soop M, Nygren J, Cox PB, Hendry PO, Spies C, von Meyenfeldt MF, Fearon KC, Revhaug A, Norderval S, Ljungqvist O, Lobo DN, Dejong CH; Enhanced Recovery After Surgery (ERAS) Group. Consensus review of optimal perioperative care in colorectal surgery: Enhanced Recovery After Surgery (ERAS) Group recommendations. *Arch Surg.* 2009; 144:961-9). Furthermore, urinary catheters were left in place for monitoring of urinary output in high risk patients. According to an internal audit (unpublished data), about 30% of prolonged urinary drainage was not medically justified (patient's comfort ...) and is target for further improvements.

Why only 20 % of cases receiving postoperative epidural analgesia which at least in open cases have shown important recovery effects?

v We do not foresee any more epidurals for laparoscopic colectomies according to our experience (Hübner M, Blanc C, Roulin D, Winiker M, Gander S, Demartines N. Randomized clinical trial on epidural versus patient-controlled analgesia for laparoscopic colorectal surgery within an enhanced recovery pathway. *Ann Surg.* 2015; 261: 648-53) which is in line with other reports (Levy BF, Scott MJ, Fawcett W, et al. Randomized clinical trial of epidural, spinal or patient-controlled analgesia for patients undergoing laparoscopic colorectal surgery. *Br J Surg.* 2011; 98: 1068–1078). Stoma procedures do not require epidurals at least in most instances. Most of the remaining patients had epidurals as suggested.

Importantly, although LOS is reported, we don't know why the patients were in hospital?

v LOS is indeed a problematic endpoint for ERAS as it was outlined by Maessen et al. (Maessen JM, Dejong CH, Kessels AG, et al. Length of stay: an inappropriate readout of the success of enhanced recovery programs. *World J Surg.* 2008;32: 971–975). It was not the purpose of the study to detail reasons for patients being in hospital. We use the Fiore criteria to decide on discharge (Fiore JF Jr, Bialocerkowski A, Browning L, Faragher IG, Denehy L. Criteria to determine readiness for hospital discharge following colorectal surgery: an international consensus using the Delphi technique. *Dis Colon Rectum.* 2012; 55: 416-23) but Swiss patients do not leave hospital always the day they are ready for discharge. A recent study on this purpose (submitted data) identified several reasons:

logistics (nursing home, family support not available), fear of complication or of “bloody discharge”. Although being obviously not an issue in Denmark, these reasons exist in our and other countries.

Even more important, it is mentioned that major complications were not different but there is no details or discussion on these complications or the pathogenesis of major complications of which according to the Dindo-Clavien classification some in no way are related to enhanced recovery per se, but rather to pure “surgical” factors.

v Complications of our ERAS cohort are transparent and have been published elsewhere. It was not the purpose of this paper to elude on pathogenesis of different complications. We agree with Prof. Kehlet on the fact that ERAS pathways are not likely to impact on surgical complications as it was nicely shown by the meta-analysis of Geco et al. (Greco M, Capretti G, Beretta L, et al. Enhanced Recovery Program in Colorectal Surgery: A Meta-analysis of Randomized Controlled Trials. *World J Surg.* 2014; 38: 1531-41).

Summarizing, although of potential interest, there are several methodological problems that hinder sufficient interpretation. The question raised need to be studied in a fully-implemented enhanced recovery program (the 5 key important elements compared to many of the remaining recommended ERAS factors that are less relevant for recovery).

v We continue to work hard on improving our postoperative performance in order to obtain results as in Rigshospitalet in Copenhagen. We agree that a study comparing a simplified ERAS protocol focused on the essentials such as RAPID (remove, ambulate, post-operative analgesia, introducing diet) with the entire ERAS protocol would be interesting.

Finally, regarding complications the study is underpowered.

v We agree that the sample size is insufficient to detect minor differences of complications. This limitation was clarified in the methods section.

Reviewer 3: Marielle M.E. Coolsen

1. This study shows better outcome than hypothesized and the authors and caregivers in the Lausanne University Hospital are to be complemented for that. However, the major drawback of this study may be that results cannot be reproduced in hospitals where ERAS has not been fully implemented and practiced by each caregiver or in hospitals where staff/services are not as abundantly present and available during the weekend days. Although the authors have already highlighted this in the discussion, in my opinion, it should be stated more clearly in the conclusion of the abstract as well.

v Staffing of medical and nursing team was detailed under methods as requested. We hypothesize that a well standardized pathway (like ERAS) might help to cope with limited resources on weekends or in general. We added a paragraph to the discussion according to Prof. Coolsen's comments.

2. Please provide additional information in table 1: specify the kind of surgical procedures performed. So, what is the number of rectal and colonic resections and the ratio in both groups?

v The requested information was added to the table.

3. The authors state that ERAS is applied in accordance with the published ERAS guidelines for colonic and rectal surgery. Although a table in reference 15 probably explains a bit, Figure 1 is unclear to me and raises some questions:

- It seems that 95% of patients in both groups have received oral bowel preparation. ERAS guidelines state that oral bowel preparation should be avoided in colonic surgery. So does this mean 95% of the procedures were rectal resections? Or did patients undergoing colonic resections also receive oral bowel preparation?

- It looks like 95% of patients in both groups received a nasogastric tube postoperatively. I assume

this should be NO nasogastric tube?

- ERAS guidelines state that resection site drainage should be avoided in colonic surgery and only be carried out on indication in rectal surgery. Did almost 80% in both groups receive drains?
- On What what day was urinary drainage/IV fluid infusion terminated in both groups?
- "Energy intake on day of surgery postoperative". Is that >600 kcal a day?
- Mobilisation at POD..., is that more than 6 hours a day?

v We apologize for this confusion and complemented the figure's legend in order to clarify. Definition of ERAS items follow exactly the published guidelines (Gustafsson UO, Scott MJ, Schwenk W, et al. Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS((R))) Society recommendations. World J Surg. 2013; 37: 259-84; and Nygren J, Thacker J, Carli F, et al. Guidelines for perioperative care in elective rectal/pelvic surgery: Enhanced Recovery After Surgery (ERAS((R))) Society recommendations. World J Surg. 2013; 37: 285-305) as referenced. Compliance for every individual item was documented as yes or no. NO bowel preparation was thus compliant as NO post-OP nasogastric tube. Ideally, all bars in Figure 1 should hence mount to 100%.

4. Line 51: "did not observed" should be "did not observe".

v Spelling error was corrected

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Nader Francis Yeovil District Hospital
<b>REVIEW RETURNED</b>	25-Jun-2016

<b>GENERAL COMMENTS</b>	I have considered this manuscript and overall it is well written and is addressing a practical and relevant clinical question in ERAS. There is only one comment which I would like the author to address more directly, which is related to the reasons, from their point of view of achieving the "good outcome" of the patients received ERAS care over weekends compared to those were operated earlier on the week. The authors pointed out to the differences in the level of staffing in their health care system but there was still clear reduction of staffing at weekends even in the Swiss Heath Care and I think it would be more educational if the authors could explain more how they have achieve their results. I was expecting the authors to explore other elements of ERAS such as patient education and ownership of their recovery particularly in an established Programe such as in the authors' institution. Also, I wonder if the authors could explain more on the model of staff training and education across all levels of health care professionals and the rota planning of the level of staffing for weekends. This would basically provide the readers with a model that help them to adopt to achieve this high level of ERAS care despite short staffing over weekends.
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<b>REVIEWER</b>	Henrik Kehlet Rigshospitalet, Copenhagen University, Denmark
<b>REVIEW RETURNED</b>	09-Jun-2016

<b>GENERAL COMMENTS</b>	Thanks for the revision which I unfortunately don't think answer the methodology question with the paper. A lot of arguments are made from the ERAS collaboration where the compliance always has been a problem especially regarding the implementation of the important postoperative items of the ERAS protocol (as emphasized by others:
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	<p>Bakker et al., Surgery 2015;157:1130-6).          Regarding the discussion of urinary drainage, the manuscript clearly shows the problem by mixing rectal and open procedures where I agree, as shown repeatedly, that low rectal operations require longer urinary drainage. However, the argument that “urinary catheters were left in place for urinary output in high risk patients” is unspecific without further details.</p> <p>Regarding epidural analgesia used in 20 % of cases, the authors’ response only focuses on laparoscopic colectomies where there is an international agreement that epidurals are not necessary. However, only about 50 % of their operations were done laparoscopic, so there is still a major difference between 20 % overall epidural use, since 50 % of the operations apparently were open? – which was my question. However, table 1 is unclear mentioning that about 30 % were open? (50 % lap vs 30 % open?) What about the stoma patients?</p> <p>The main problem is length of stay, which is not explained. The response letter repeatedly argues that Danish experience is different from the ERAS collaboration. This is unfortunate, since my arguments are not based on Danish experience alone; several other publications have shown very short length of stay with a fully implemented ERAS program with both laparoscopic and open procedures (literature not quoted in the manuscript).</p> <p>In summary, although the topic is of general interest, the question about the impact of weekday on an enhanced recovery pathway cannot be answered sufficiently without a fully implemented procedure-specific evidence-based postoperative pathway. Therefore, although of some interest from the present results, a more detailed discussion about the week-day of surgery vs the compliance problems vs. the outcome question is required.</p>
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<b>REVIEWER</b>	Marielle M.E. Coolsen MUMC+, Maastricht The Netherlands
<b>REVIEW RETURNED</b>	04-Jun-2016

<b>GENERAL COMMENTS</b>	The reviewer completed the checklist but made no further comments.
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### VERSION 2 – AUTHOR RESPONSE

Reviewer 1: Nader Francis

I have considered this manuscript and overall it is well written and is addressing a practical and relevant clinical question in ERAS. There is only one comment which I would like the author to address more directly, which is related to the reasons, from their point of view of achieving the "good outcome" of the patients received ERAS care over weekends compared to those were operated earlier on the week. The authors pointed out to the differences in the level of staffing in their health care system but there was still clear reduction of staffing at weekends even in the Swiss Health Care and I think it would be more educational if the authors could explain more how they have achieve their results. I was expecting the authors to explore other elements of ERAS such as patient education and ownership of their recovery particularly in an established Programme such as in the authors' institution. Also, I wonder if the authors could explain more on the model of staff training and education across all levels of health care professionals and the rota planning of the level of staffing for weekends. This would basically provide the readers with a model that help them to adopt to achieve this high level of

ERAS care despite short staffing over weekends.

- We thank Prof. Francis for the opportunity to explain our point of view. First of all, it is important to mention that most of our nursing staff is dedicated staff, remaining in the Department for several years, and thus through the ERAS implementation and consolidation process. In some way, they build the “backbone” of our nursing staff since as they fulfill important teaching tasks. In order to ensure a continuity of care through the weekend, senior and junior staff members are paired whenever possible, likewise for medical and nursing staff. Periodically, every 6 months at least (after arrival of new colleagues), the junior medical and nursing staff is instructed by senior surgeons and the dedicated clinical ERAS nurse (V. Addor, co-author) to update all caregivers on ERAS care during Institutional staff meetings. Hence, new colleagues are instructed during the first week after their arrival in the facility. Further, new evidence or institutional publications are presented during surgical staff meetings and journal clubs. Obviously, hebdomadal meetings of ERAS members (surgeons, anesthesiologists and senior nurses) take place to discuss related issues or problems. Combined with the previous explanations in the first response letter (i.e. high staffing level), we believe that these measures contribute to the continuity of care through the weekends. These points have been emphasized in the discussion section.

Reviewer 2: Henrik Kehlet

A lot of arguments are made from the ERAS collaboration where the compliance always has been a problem especially regarding the implementation of the important postoperative items of the ERAS protocol (as emphasized by others: Bakker et al., *Surgery* 2015;157:1130-6).

- We agree with Prof. Kehlet that compliance of the protocol is not yet optimal in our patients despite the intensive formal training and implementation program. A very complete and honest reporting of our performance might provide one explanation for “worse results” than some other centers. Furthermore, we encounter similar problems especially for the postoperative items as reported also from the Dutch and Swedish experience (Maessen J, et al. A protocol is not enough to implement an enhanced recovery programme for colorectal resection. *Br J Surg.* 2007; 94: 224-31; Gustafsson UO, et al; Enhanced Recovery After Surgery Study Group. Adherence to the enhanced recovery after surgery protocol and outcomes after colorectal cancer surgery. *Arch Surg.* 2011; 146: 571-7). We discussed this topic in the discussion and under limitations.

Regarding the discussion of urinary drainage, the manuscript clearly shows the problem by mixing rectal and open procedures where I agree, as shown repeatedly, that low rectal operations require longer urinary drainage. However, the argument that “urinary catheters were left in place for urinary output in high risk patients” is unspecific without further details.

- We agree that we report on a heterogenous cohort of patients, which however pictures the daily activity at our Institution. Like Prof. Kehlet, we were interested in compliance rates regarding Foley catheter removal. Briefly, we found that Foley catheters were removed later than on POD 1 in 32% of patients after right or left colectomies (submitted data). In major abdominal surgery, perioperative urinary catheters help to guide volume resuscitation and to maintain hemodynamic stability (Baldini G, Bagry H, Aprikian A, Carli F. Postoperative urinary retention: anesthetic and perioperative considerations. *Anesthesiology.* 2009;110(5):1139-57). Intuitively, urinary catheters were thus left in place in patients who needed close surveillance in intensive or intermediate care wards, especially on the weekend. However, recent evidence questions the utility of monitoring urinary output for volume resuscitation (Glassford NJ, Jones SL, Martensson J et al. Characteristics and expectations of fluid bolus therapy: a bi-national survey of acute care physicians. *Anaesth Intensive Care.* 2015;43(6):750-6). We therefore took measures to apply the same protocol for early catheter removal according

to the most recent ERAS guidelines (Gustafsson UO, et al. Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations. World J Surg. 2013; 37: 259-84; Nygren J, et al. Guidelines for perioperative care in elective rectal/pelvic surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations. World J Surg. 2013; 37: 285-305) for all patients irrespective of the day of surgery.

Regarding epidural analgesia used in 20 % of cases, the authors' response only focuses on laparoscopic colectomies where there is an international agreement that epidurals are not necessary. However, only about 50 % of their operations were done laparoscopic, so there is still a major difference between 20 % overall epidural use, since 50 % of the operations apparently were open? – which was my question. However, table 1 is unclear mentioning that about 30 % were open? (50 % lap vs 30 % open? What about the stoma patients?

- We clarified information provided in Table 1 as requested and we clarify hereby that only 26.8% of our cohort underwent a planned open resection requiring an epidural according to ERAS guidelines. Our policy adheres thus to ERAS guidelines and recent publications (including our own published data):

- 1) No epidurals for laparoscopic cases and stoma procedures.
- 2) Epidurals for most open cases except for patients with contraindications including patients' refusal.
- 3) For the remaining patients, new pain management strategies have been exerted, in particular intravenous lidocaine infusion or ultrasound guided transversus abdominis plane (TAP) blocks, and thus they account for some of the open procedures of our cohort.

These points have been clarified in the methods section.

The main problem is length of stay, which is not explained. The response letter repeatedly argues that Danish experience is different from the ERAS collaboration. This is unfortunate, since my arguments are not based on Danish experience alone; several other publications have shown very short length of stay with a fully implemented ERAS program with both laparoscopic and open procedures (literature not quoted in the manuscript).

- Length of stay is a problematic endpoint as it depends on multiple factors (Maessen J, Dejong CH, Hausel J, Nygren J, Lassen K, Andersen J, Kessels AG, Revhaug A, Kehlet H, Ljungqvist O, Fearon KC, von Meyenfeldt MF. A protocol is not enough to implement an enhanced recovery programme for colorectal resection. Br J Surg. 2007; 94: 224-31). We agree that our LOS is longer than the one reported by other groups. Several references (Levy BF, Scott MJ, Fawcett WJ, Rockall TA. 23-hour-stay laparoscopic colectomy. Diseases of the colon and rectum 2009; 52: 1239-43; Keller DS, Stulberg JJ, Lawrence JK, Delaney CP. Process control to measure process improvement in colorectal surgery: modifications to an established enhanced recovery pathway. Diseases of the colon and rectum 2014; 57: 194-200; Andersen J, Hjort-Jakobsen D, Christiansen PS, Kehlet H. Readmission rates after a planned hospital stay of 2 versus 3 days in fast-track colonic surgery. The British journal of surgery 2007; 94: 890-3) were added in the discussion as requested. However, our hospital stay is below the benchmarking of all centers included in the international ERAS data base comprising over 30'000 patients and thus reflecting the current situation. Nonetheless, we agree that there is room for improvement.

In summary, although the topic is of general interest, the question about the impact of weekday on an enhanced recovery pathway cannot be answered sufficiently without a fully implemented procedure-specific evidence-based postoperative pathway. Therefore, although of some interest from the present results, a more detailed discussion about the week-day of surgery vs the compliance problems vs. the outcome question is required.

- The discussion was expanded as suggested. Prof. Kehlet repetitively suggests that our reports

reflect the experience of a not fully implemented ERAS pathway because our compliance is not optimal. We cannot follow his argumentation in this point as our results are in line with other reports and the large prospective ERAS database as quoted above. We report therefore the findings of a formally trained ERAS center applying the full recommended ERAS protocol as best as possible in our daily routine.

Reviewer 3: Marielle M.E. Coolsen

No comments (satisfied with revision)

- We thank Prof. Coolsen for accepting our revised version.