Reviewer's report

Title: Improved Analgesia and Reduced Post-Operative Nausea and Vomiting after Implementation of an Enhanced Recovery After Surgery (ERAS) Pathway for Total Mastectomy

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Reviewer: Michael Grant

Reviewer's report:

Chiu and colleagues have submitted the manuscript entitled "Improved Analgesia and Reduced Post-Operative Nausea and Vomiting after Implementation of an Enhanced Recovery After Surgery (ERAS) Pathway for Total Mastectomy" for consideration for publication. Therein, they have outlined various process measures associated with the implementation of an ERAS program for mastectomy at their institution. They have performed a "before/after" analysis to assess the primary endpoint of opioid consumption and several associated secondary outcomes. Based upon the results of their study, they conclude that a concerted ERAS program led to a significant reduction in perioperative opioid administration, better pain control and lower rates of PONV. The authors should be commended for development of a comprehensive program for perioperative care. In addition, the manuscript is well written and appropriately organized.

I am generally torn as to how to officially handle this submission. As a stark proponent of ERAS in virtually all settings, I am encouraged to see this kind of program extended to a virtual outpatient setting. But this "study" has many of the limitations that are regularly said of ERAS-based studies: it is incredibly confounded by the nature of the analysis, the non-uniformity of the various process measures, the lack of control for intermixing various forms of regional analgesia and the vagueness of how process measures are described in the methods. Taken specifically as an "intention-to-treat" quality improvement product, the program seems quite successful. But the authors haven't written the text to suggest this is a patient quality initiative, it is written as if analyzed by traditional interventional research. Because the tone is very much the latter, I am disappointed in the approach. A simple t-test or comparison of medians is inappropriate in this setting - it would have been better to construct a formal logistic regression analysis to account for baseline differences or even process measure non-compliance. But there are far too few numbers of patients to facilitate this kind of analysis (350 total is far too few). The primary objective is a bit of a quizzical selection and needs further justification. In general, I think this would be far more successful if rewritten as a description of a quality initiative rather than basing results on traditional research standards. My further comments can be reviewed below:
Major Comments:

1. At its heart, this represents a before-after analysis, which is fraught with numerous analytical issues. First, it would be difficult, if not impossible, to control for system-level changes, cultural shifts or unrecognized process measures that might have impacted the outcome. Therefore, it would be difficult to know what part of the ERAS bundle was associated with the improvement in outcomes. I wonder if the authors might acknowledge this further in their discussion. Page 7, Ln 131-132. This statement is incredibly important: the hospital that housed the program made a MAJOR systematic transition to a 23hr hospital at the same time of this program's inception. That confounder alone requires immediate attention.

2. The concept of developing an ERAS pathway for an outpatient procedure is a foreign one. While this reviewer supports it in principle, it will fall upon much scrutiny by other readers as ERAS pathways are traditionally developed for patients with lengthier stays. It might be helpful to instruct the reader further as to why such a pathway is needed at all for a patient who will undergo only a 23 hour stay - improved PONV/analgesia leading to what...? The authors mention long term postsurgical pain as part of their rationale in the introduction, which is nice, but this study certainly isn't powered or designed to examine that endpoint.

3. The introduction is too long and the final paragraph reads far more like it belongs in the methods section instead of the introduction. My suggestion would be to truncate the intro significantly, provide strong rationale (see point 2 above) for ERAS in this setting, identify the primary endpoint and justify its selection. This lattermost point is vital: why should a provider care about opioid consumption if these patients go home at 23 hours?

4. The data with respect to a "trend toward decreased length of stay" is very misleading. Having data that is almost significant doesn't predict the nature of the subsequent data. It is just as likely that you could enroll 100 more patients and your p-value goes to 0.2 as it is for the p-value to become significant. Also, the entire nature of the hospital changed when ERAS was implemented and it is frankly impossible to know if the effect is a result of the analgesia/PONV or an effect of simply shifting to an "ERAS mentality". I think each is just as powerful, but the way the current data is presented is potentially misleading.

5. The discussion is very long and should be truncated significantly. I would recommend shortening the discussion on regional analgesia to a single paragraph. Furthermore, no
regression analysis was performed and therefore any "subgroup" analysis on individual interventions isn't appropriate in this setting. Individual effect sizes of process measures is far more informed through the use of logistic regression. Furthermore, logistic regression would be one way to ensure that patient and and surgical covariables aren't specifically impacting the results of the initial analysis. This is problematic due to the low overall number of included patients in the trial.

Minor Comments:

1. Why did the authors select 98 patients in the ERAS group and 276 in the pre-ERAS group? Where/how were these numbers derived? Perhaps a power analysis might help inform the reader that enough patients were enrolled to examine the primary endpoint.

2. Methods - how did you define "avoidance of prolonged fasting"?

3. Methods - was TIVA standardized? I see it excluded inhaled agents, but did it include opioids? Propofol? other?

4. Methods - the use of postoperative analgesics needs to be better articulated: were non-opioids scheduled or PRN? If PRN, were they given prior to hydromorphone or other opioids? How was the decision made to provide opioids? Via failure of non-opioids or ad hoc?

5. Methods - did the patient receive Pecs or Paravertebral by any specific consideration? Meaning - was this just provider preference? How did outcomes change depending on which was selected?

6. Methods - where did the author derive their opioid conversion approach?

7. Methods - in general, it would be helpful to be explicit in how various process measures were defined and isolate those description to 1-2 paragraphs within the methods section. As it currently reads, the introduction, methods and even discussion all provide "new" information regarding the specifics of process measures.

8. Discussion - the first line should have the word feasibility removed. This was not a feasibility study - this was an outcomes study. As a result, you aren't describing if this program can exist, you are attempting to show that real results extend from your work.
This is an important distinction. It is also perhaps the primary issue a reader may take with interpretation of the results: is this a quality study or a traditional intervention investigation? In order for ERAS studies to take a step forward in acceptance, the approach taken to their analysis should be exacting in nature.

9. Discussion - there is a claim that there were "minimal changes in workflow". Can you please expand upon this? I don't see evidence of this - the authors state that the entire hospital was transitioned to a 23 hour hospital. I can think of no greater workflow alteration than that.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

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