Reviewer’s report

Title: The occurrence of adverse events in relation to time after registration for coronary artery bypass surgery: a population-based observational study

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Reviewer: Annie Laurie W. Shroyer

Reviewer’s report:

The co-author team of the manuscript, entitled “The occurrence of adverse events in relation to time after registration for coronary artery bypass graft (CABG) surgery: a population-based observational study”, are to be commended for addressing this critically important question. As Canada explicitly coordinates surgical wait lists to most efficiently utilize their limited resources available, the purpose of their study was to examine the impact of delays in cardiac surgery wait times upon adverse events.

Specifically, this research team was interested in understanding if longer delays for patients (both urgent and non-urgent) led to increased rates of emergent surgical procedures and/or deaths for patients wait-listed. For British Columbia Cardiac Registry (BCCR) patients’ awaiting a CABG procedure at one of the 4 regional cardiac surgery centers, this well established database included over 12,000 non-emergent patients that had been wait-listed for a primary CABG-only procedure during the 13 year period from 1/1992 to 12/2005. The patients were classified at registration as urgent (i.e., procedure should be performed within 1 week), semi-urgent (i.e., procedure should be performed within 6 weeks), or non-urgent (i.e., procedure should be performed within 12 weeks).

All wait listed patients had a catheterization performed to evaluate for the appropriateness of CABG procedure planned. The other study record inclusion/exclusion criteria used were reasonable. As very minor point, the co-authors made the following statement which likely should be removed (as it is not relevant to the study period previously specified): “We also excluded 1,452 records of patients that were registered in 1991”.

The methods used are appropriate, as well as well described. Additional analytical approaches are suggested, as noted in the questions below, to explore how best to facilitate future health policy recommendations using this study’s database findings.

The BCCR patient data was linked to the Canadian Institute for Health Information (CIHI) discharge database to identify the study endpoints, which included: survival to elective CABG surgery, requirement for an emergent CABG surgery, or death while on the wait-list. Additionally, census data based on patient-specific postal codes were used to identify regional patient characteristics.
For the authors' review and consideration, the following questions have been raised:

1. **Registration Status Classification Accuracy**: For the sub-group of survivors to elective CABG surgery, was the initial registry “status” classification assigned [that is, their urgent (i.e., procedure should be performed within 1 week), semi-urgent (i.e., procedure should be performed within 6 weeks), or non-urgent (i.e., procedure should be performed within 12 weeks)] appear to have been generally achieved? Specifically, the following table would be helpful to add:

<table>
<thead>
<tr>
<th>Urgent</th>
<th>Semi-Urgent</th>
<th>Non-Urgent</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Died Prior to Receiving CABG Surgery</td>
<td>Already on table 2.</td>
<td>Already on table 2.</td>
<td>Already on table 2. #/#%</td>
</tr>
<tr>
<td>Received Emergent CABG Surgery</td>
<td>Already on table 2.</td>
<td>Already on table 2.</td>
<td>Already on table 2. #/#%</td>
</tr>
<tr>
<td>Received Elective CABG Surgery</td>
<td>#/#%</td>
<td>#/#%</td>
<td>#/#% #/#%</td>
</tr>
</tbody>
</table>

For patients surviving to an elective CABG procedure, number of days awaiting surgery Mean (STD) and Median (IQ range) Mean (STD) and Median (IQ range) Mean (STD) and Median (IQ range) Mean (STD) and Median (IQ range)

2. **Rationale for 52 Week Follow-up Period**: Why did the coauthor team restrict their analysis to the first 52 weeks following registration? Given that censoring might used for records with partial data available, perhaps a life-table approach (e.g., comparing the log-rank tests for Kaplan-Meier curves) be performed to compare the urgent, semi-urgent, and non-urgent patients surviving to an elective CABG procedure?

3. **Major Adverse Cardiovascular Events (other than Death)**: Might it be possible to identify wait listed patients where other major adverse cardiovascular events (e.g., a non-fatal myocardial infarction or a percutaneous coronary intervention) may have occurred to augment the analysis currently performed and potentially explain findings within the non-urgent patient sub-group?

4. **Patient Choice to Delay Surgery**: Might it be possible to identify the sub-group of patients where their own choices (rather than system-based causes for delays and/or resource constraints causing delays) had delayed the timing for their own elective CABG procedure? If so, might the analysis please be re-run without patients that choose a delay (e.g., daughter was in a wedding in the coming month)?

5. **Clinician Choice to Delay Surgery**: Potential confounding may be (at least in part) be due to the severity of coronary disease and/or recent coronary events that have occurred. For example, a patient that recently had an acute MI may be purposefully delayed for CABG to “cool off” prior to the surgery. Might it be possible to identify the sub-groups of patients where clinician choices (to purposefully delay the surgery beyond a certain time frame – such as 10 days) might be identified? If so, might the analysis please be re-run without these
patients with a purposeful clinical delay (e.g., cool off for an acute MI patient)?

6. Surgical Center-Based Effects: Might there be center-specific referral effects, that is a center that patients and/or their clinicians would prefer to wait to have their procedure performed at this facility? If so, might center be a potential regression model variable to account for referral variations and/or mix of the different severity of patients that are commonly treated across these four facilities?

7. Patient Characteristics Across Status Categories: Were the patient profiles that received emergent surgery across the classifications for urgent, semi-urgent, and non-urgent status similar or different? Of the patients that received emergent surgery, what proportion survived? What was the combined rate for all deaths that occurred – that is those occurring while on wait list and/or related to a surgical procedure performed (i.e., after emergent, urgent, semi-urgent, and/or non-urgent surgery)?

8. Threshold Analysis: Although this study found that the non-urgent and semi-urgent patient sub-groups that waited longer were more likely to die while still on the wait list, was there any wait time threshold (e.g., a number of days that patients waited) that posed an increased risk of death? For example, did the originally proposed status time period (i.e., 1 month, six weeks, or 12 weeks) appear to be actual thresholds that posed any additional threat of death for wait-listed patients? To clarify, can a threshold analysis be used to verify that the time frames identified for the different status groups [that is, for the semi-urgent (i.e., procedure should be performed within 6 weeks), or non-urgent (i.e., procedure should be performed within 12 weeks) patients] appropriately established? As the basis for future health policy discussions, based on this study’s findings might there a point at which the co-author team might recommend that all non-urgent patients should receive a CABG (e.g., not longer than 12 weeks?) to assure that there is no difference with the semi-urgent patient group rates?

9. Seasonality of Wait Time Delays: Might there be a seasonality effect (e.g., a time of year impact) associated with extended wait time delays? For example, are delays longer if the patient is placed on the registry in December versus in April?

10. Care Received Outside of Canadian Health Care System: Might potentially patients received a CABG procedure outside of the Canadian health care system (e.g., paying for this separately)? If so, might the out-of-system CABG care be estimated as to the volume as well as impact on the BCCR? Although access to out-of-system care may be related to the socio-economic decile, it was unclear if there may be a mechanism to measure this separately via the registry information currently gathered.

11. Predictors of Death on Wait Listing: To augment the analyses performed, might the coauthors build a categorical logistic model that predicted the endpoints for 1) survival to elective CABG; 2) survival to emergent CABG; or 3)
death on the wait list? If so, then the relative importance of a patient’s initial registration status (urgent, semi-urgent, and non-urgent) could be evaluated in context of their other patient-specific risks (e.g., age) and center-based challenges (e.g., center-specific effects).

As a small point, it is hard to read the figures given the confidence intervals that are plotted. Hence, either color coding or removing the confidence interval curves may be helpful to consider to easily interpret the “take-home” messages for these two figures.

In summary, this paper is very well written and addresses an important question raised – that is what is the impact of extended CABG wait times upon patient outcomes. The discussion and conclusion, as well as the limitations identified, are written in a manner to add to the knowledge in this field. The only concern of this reviewer is that the co-author team stopped short of using the data available to identify potential opportunities to improve the system that is in place – by identifying ways to improve the status classification system (e.g., how to set expectations for wait delays for urgent, semi-urgent, and non-urgent patients) as well as to identify if a safety threshold might exist – beyond which no patients should be requested to ever wait.

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests