Reviewer's report

Title: Risk Factors of Short-term Mortality after Acute Nonvariceal Upper Gastrointestinal Bleeding in Patients on Dialysis: A Population-Based Study

Version: 1 Date: 6 September 2012

Reviewer: Eric Weinhandl

Reviewer's report:

Abstract

It would be reasonable in the Methods to explicitly declare that this study is restricted to the subset of patients in the USRDS with Medicare coverage.

“The joint ability of all factors captures to predict mortality was modest (c=0.68).” Two notes: (1) Consider replacing "captures" with "captured". (2) Consider replacing "predict" with "discriminate", as the c-statistic is properly a measure of discrimination.

Introduction

This section is lengthy and much of the content in the second paragraph is better suited for the Discussion, in my opinion.

Methods: Data Source

The USRDS does NOT contain claims for "almost all patients." This is an overstatement.

Methods: Identification of ANVUGIB episodes

Please list all diagnosis codes used to ascertain events, even if only in an online appendix. It is not clear to me that the text currently includes all codes used by Targownik et al and the reader should not be expected to refer to that study for full details of the methods used here.

I think that the audience would benefit from a clear description of types of claims searched (inpatient, outpatient, home health, hospice, skilled nursing facility, physician/supplier) and which types to which the label "outpatient" refers here.

Regarding esophagogastroduodenoscopy, did the authors search outpatient facility claims for the diagnosis code and physician/supplier claims for the procedure code? Or did the authors merely search physician/supplier claims for the inclusion of both applicable diagnosis and procedure codes? (The latter may be a sufficient approach, so please do not overinterpret my use of the word "merely".)

Please, at some point, clarify that in the cases of two outpatient claims or two
events in a 30-day period, that the latter claim or event was used as the index date marking the beginning of follow-up.

Methods: Candidate predictors

Regarding prior ANVUGIB episodes, I am not religiously opposed to the approach here, but the authors should alert the reader (in the Discussion) to the fact that the accuracy of this covariate is, by construction, confounded by the duration of Medicare coverage prior to the index event. Later, I see that no history of ANVUGIB is a risk factor for death. Is it truly? Or are incident patients, without historical claims indicating ANVUGIB, at increased risk of death?

Methods: Statistical Analysis

I am unclear about which interaction were assessed, without surmising the approach from the results in Appendix 1. I will remain agnostic about Whether this is a problem.

Results

The reported prevalence of hypertension is dubious. Consider whether this comorbidity possesses sufficient face validity so as not to detract from the quality of the study.

"The most common cause of bleeding..." A strong statement, in my opinion. A truer interpretation of the data is this: "The diagnoses most commonly identifying ANVUGIB episodes were..."

In addition to reporting c, the authors might also consider reporting a pseudo R^2 statistic, as many exist for logistic regression. Discrimination is one piece of the puzzle, but it is only piece. Also, it would be interesting to see if c itself is greater simply when age is parameterized as a continuous factor rather than categorical factor. The presented model have modest discrimination, but the measured covariates themselves may have been discriminatory capability than has been surmised to this point.

The authors do not clearly identify whether "other" race is a risk factor. It's clear to me that white race is a risk factor with respect to black race, but the same cannot be said for white race vis a vis other race.

I think that vintage should be more granular than what has been constructed. Patients with vintage < 3 yr are not a homogeneous group. Vintage < 1 yr is substantially different than vintage between 1 and 3 yr.

Regarding "Bleeding likely peptic ulcer related"; is this covariate defined by the presence of a diagnosis code for peptic ulcer with hemorrhage, as displayed in Table 2?

Regarding hospitalized episodes, it would be helpful to see a sensitivity analysis that delineates whether this risk factor is primarily a function of in-hospital death or whether the risk persists in those who are discharged alive.
Also, it would be interesting to see this analysis repeated in the mutually exclusive subsets of patients who were hospitalized and who were NOT hospitalized on the index, so as to see whether risk factors are similar.

Discussion:

The authors note that the liver disease was the most prominent comorbidity, on the basis of adjusted ORs (I would surmise). However, cancer is virtually indistinguishable on the basis of OR magnitude. The authors might consider some discussion of this aspect.

The discussion of CAD and ischemic heart disease is wandering and could be reasonably shortened. I think that the adjusted OR for CAD here may be attenuated because of complex causal pathways among histories of CV events (e.g., MI causes HF, so simultaneous adjustment for history of MI and history of HF blocks the effect of CAD). I suppose it's fair to say that I have a difficult time interpreting this risk factor too rigorously.

This PD vs HD issue is exactly the sort of contrast that I'd like to see replicated in the subset of patients who are hospitalized and who are not hospitalized on the index date.

I think that the discussion of prior ANVUGIB is great, but if the authors want to devote this much attention to the topic, then I think that the case of refining the definition of history of ANVUGIB is even stronger. I wonder about how much of this effect may be driven by "history of" is a marker for readmission following survival from the previous episode (which, as the authors note, is survivor bias). I am increasingly uncomfortable with searching claims back to 1996, when patients do not all have the same duration of claims history.

The limitation about applicability to patients dialyzing for less than 1 year now has been wondering about the cohort definition in a new way. Did the authors exclude patients with < 1 yr of dialysis at the time of ANVUGIB? While it’s true that non-elderly patients would often be implicitly excluded by requiring 1 year of Medicare coverage, elderly patients with Medicare prior to ESRD would not necessarily be excluded. On this note, the decision to require an entire year of claims to ascertained comorbidity ---- in my humble opinion ---- is up for some debate. I suspect that conclusions would be very similar (and N would be larger) if the authors had simply required 6 months of prior Medicare. The authors might still consider such a revision, depending on appetite for further analysis.

Given the data source, it's curious to me that in a study about bleeding, that the authors made no attempt to ascertain data about anemia management, including EPO doses, Hb concentrations, and transfusion events.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable
**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests