Reviewer’s report

**Title:** In-hospital mortality in stomach cancer surgery: patient factors, clinical factors, and relationship with volume of interventions

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**Reviewer:** Salvador S Peiró

**Reviewer’s report:**

**Major Compulsory Revisions**

1. This is an interesting paper whose aims are: 1) to estimate the in-hospital mortality rate in surgery for gastric cancer in different hospitals from 4 regions -not in regions, as stated in the manuscript- of Spain; 2) to identify factors associated with greater in-hospital mortality; and 3) to analyze the possible link between surgery volume and in-hospital mortality. This last objective is the one of most interest, since shedding light on this issue has major implications in healthcare strategies, and in the decision of whether or not to centralize surgery for cancer of the stomach in a few, highly specialized hospitals. However, the validity of comparisons of rates of risk adjusted clinical outcomes as measures of performance can be biased by the exclusion of important risk factors from predictive equations, the improper use of hospital-acquired complications as risk factors, and inconsistent reporting of valid risk factors included in predictive equations [Michael Pine et al. Hospital Mortality Risk Adjustment Using Claims Data. JAMA. 2007;297:1984]. The analysis as it was conducted in this paper presents some of these important limitations that do not lead to a clear conclusion. Some of these limitations are related to the source of data used. Others, however, can be controlled, at least in part, with additional or different analysis and with the provision of further information.

2. The development of the three objectives is conditioned by limitations associated with the quality of the source of data used. The Minimum Basic Data Set (MBDS) at Hospital Discharge is an administrative database that is subject to biases related to the volume of information registered. Not only can the information included in the MBDS vary from one hospital to another, there can be biases induced by the inclusion of retrospective information, so that the inclusion of diagnostic notes can vary according to the severity of each patient, the presence of associated pathologies and by outcomes themselves. (See Jencks S et al. Assessing hospital-associated deaths from discharge data. The role of length of stay and comorbidities, JAMA. 1988; 260:2240-6 and Librero J, Peiró S. Do chronic diseases prevent intra-hospital mortality? Paradoxes and biases in information about hospital morbidity. Gac Sanit. 1998;12:199-206 about comorbidity biases in the MBDS and Iezzoni LI et al. Comorbidities, complications, and coding bias. Does the number of diagnosis codes matter in predicting in-hospital mortality? JAMA. 1992; 267:2197-203 about retrospective information biases). These biases are evident in this study in that chronic
morbidity (Charlson =3) appears to be a protection factor compared to Charlson 2, and it would be important to know whether these factors differed between the different types of hospitals. We believe this study needs to provide information about the number of diagnostic notes included (number of secondary diagnoses) and their distribution in terms of the volume of surgery for stomach cancer in each hospital.

3. In-hospital mortality is an outcome that is extraordinarily dependent on the length of stay (LOS). The more days the patient remains hospitalized, the greater the probability of being identified as an in-hospital mortality case upon death. This bias is such that hospitals with a shorter LOS also have fewer (in-hospital) deaths than hospitals with a longer LOS. If a hospital has an average stay of ten days for these patients, mortality is counted until the tenth day; these hospitals have a clear advantage over those whose average LOS is twenty days. With the distribution of stays described in this study (LOS 25±18; range: 1-291) the impact of this bias is likely to be very high. It, therefore, seems appropriate to provide information about the LOS in each hospital and relate this data to the hospital's volume of cancer stomach surgery.

4. It would be useful to see a table comparing surgery volume and certain patient characteristics. Table 1 could be replaced by a table with more information about the distribution of risks and the quality of information about the three hospital groups.

5. Additionally, the use of the Cox proportional hazards models rather than regression logistics or the chi-squared analysis would contribute to palliating the differences in length of stay. While the Cox models cannot control for all the problems associated with the bias described above, they are a better alternative to ignoring the time each patient is remains in hospital. But it should be borne in mind that the length of stay is ambivalent in relation to the quality of the care received (greater LOS may be the result of complications, but also may be the cause of complications such as nosocomial infections). Obviously, it would be much better to have information about mortality at 30 or 60 days, but this outcome is not available through the MBDS. There are also other ways to manage this LOS bias (see Miyata H et al. Performance of in-hospital mortality prediction models for acute hospitalization: Hospital Standardized Mortality Ratio in Japan. BMC Health Serv Res. 2008; 8:229).

6. For the selection of the cases included in the study, the authors appear to have used the ICD9CM codes for all 151 diagnoses (which excludes in situ stomach carcinoma, code 230.2), and the codes for procedures 43.0 to 43.9 that they define as “total or partial gastrectomy”, but that include procedures that are exploratory (43.0 Gastrotomy) as well as palliative (43.11 and 43.19 gastrostomy, a procedure performed basically for nutritional support). Mortality derived from the procedure in these cases is very different from the parameters the authors are studying (although in the case of palliative procedures mortality may be associated with the patient's condition). It is not clear, therefore, that these procedures should be included when they are performed in one-off situations (and in all events, they should not be refered to as gastrectomies). The authors
should either justify or case selection methods. They should, further, clearly describe the volume of patients receiving these procedures in each type of hospital, since less specialized hospitals may perform procedures differently than those with high volumes of stomach cancer surgery.

7. To adjust for risks, the authors used surgical factors, patient comorbidities, factors related to the severity of the disease and complications. The inclusion of complications as a risk adjustment factor is inappropriate when making comparisons between types of hospitals, since complications may be associated with low quality of hospital care and to be, in fact, the cause of death. Including complications in the adjustment leads to underestimating the risk of mortality attributable to the hospital (An example would be when adjusting mortality for such variables as acute respiratory failure, a complication that may be associated with low quality hospital care. The patient is unlikely to present respiratory failure upon admission, otherwise he would not have received surgery. So, the excessively high rate of mortality derived from the onset of this complication is eliminated from the analysis of the hospital's performance).

8. Additionally, this problem is usually linked to an information bias (since if the patient dies, more complications are recorded than if he does not), which accentuates the association between the complication and death, further underestimating the risk of death in hospitals with more complications. In order to evaluate whether a hospital's surgery volume affects mortality, only diagnoses present upon admission should be considered, and those that may have arisen as a result of inadequate management of the patient, excluded. The MBDS does not provide information of this nature. Clinical judgement should, therefore, be used to discard from the adjustment those complications that were probably not present upon admission (respiratory failure, renal failure, fluid and electrolyte disorders, acute myocardial infarction, etc.), and contemplate only those that were (diabetes, hypertension, diverticulosis, etc).

9. The inclusion of complications that can practically be considered causes of death (63% deaths with respiratory failure, 60% with renal failure, etc.) also has the effect of saturating the logistics model, since these "independent" variables are practically identical to the "independent" variables. This aspect explains the high C-statistic in the logistics regression model. The authors should apply clinical judgement to include only secondary diagnoses present upon admission, and exclude any appearing after surgery.

10. The article does not present a table with the logistics model, although the model is partially described in the text. It would be of interest to have information about the variables that were discarded, the CI95% of the OR and other parameters.

Minor Essential Revisions

11. Page 4. Paragraph 2.1.- Although the authors describe the design as “a retrospective descriptive study” the study, in fact, is basically analytical. A more accurate description of the design would be a "retrospective cohort (based on
administrative data)", because patients are followed from admission to death or discharge.

12. Page 4. Paragraph 2.1.- The use of the term "administrative register” to describe the MBDS is confusing. A better term would be "administrative database”.

13. Page 5. Paragraph 2.4.- In-hospital mortality is defined as “death occurring during the hospital stay”. However, the MBDS includes a code for “in extremis discharge” (patients discharged alive to die in their homes), and these cases should also be considered as in-hospital deaths. The authors should explain whether they have done this.

14. Page 4. Paragraph 2.4.- The cut-off by terciles to classify the hospitals seems to have been done in function of the patients rather than of the hospitals. This cut-off point is not very clear, since it is difficult to envisage the volume of surgery that should be considered "low", "medium" or "high". Additionally, the authors do not say how many hospitals are included in each group. The authors also need to explain better the “13 volume categories corresponding to smaller ranges consisting of 10 discharges each”, as this is description is confuse.

15. Page 4. Paragraph 2.5.- The authors say that “the odds ratios and 95% confidence intervals were calculated” but this 95% is not reflected in the paper. It is also not clear what the statement about grouping cases “in volume categories with ten by ten increments” (in fact, they grouped hospitals, not cases).

16. Page 6. Paragraph 3.1.- The LOS is described as 25±18. We are not sure whether the dispersion statistic corresponds to the Standard Error parameter (correctly described as 25±18) or to the Standard Deviation parameter (in this case, which must be described as “25(18)” or “25; SD:18; range:1-291”. The SD cannot be added to, or subtracted from the mean.

17. Page 6. Paragraph 3.1.- The results of the logistics regression should be presented in a table.

18. The discussion about the limitations affecting the quality of the data should be expanded and contextualized. The way in which these limitations affect the study should be described.

Discretionary Revisions

19. The subheadings in each section of the manuscript are unnecessary.

**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:

We declare that we have no competing interests