Author's response to reviews

Title: Utilization of evidence-based treatment in elderly patients with chronic heart failure: Using Korean Health Insurance Claims Database

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TITLE: Utilization of evidence-based treatment in elderly patients with chronic heart failure: Using Korean Health Insurance Claims Database

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Response to Review
June 9, 2012

Dear BMC Cardiovascular Disorders reviewers and editorial staffs:

We would like to express our sincere gratitude for your consideration and thorough scrutiny of our manuscript. We greatly appreciate the referees’ specific suggestions and constructive comments. According to the provided suggestions, we have made some corrections and clarifications in the manuscript and have enclosed our revised manuscript together with point-by-point responses to the referees’ comments. Revised parts of manuscript are in blue text. We guarantee the accuracy of our references. We hope our revisions will be considered and accepted in the affirmative air during the further review process. Once again, we appreciate your consideration and look forward to hearing good news from you soon.

Sincerely yours,

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Comments to the Author and Author’s reply

Reviewer 1: 🌼

Methods:

1. To this reviewer is not clear if the treatments are prescribed at the discharge from hospital or by general practitioner after the discharge from hospital.

We included treatments both prescribed during the admission and outpatient clinic setting. Patients prescribed from outpatient clinic were 60.8% of total study population.

<table>
<thead>
<tr>
<th>Prescription sources</th>
<th>Person based (%)</th>
<th>Prescription based (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>inpatients</td>
<td>11346 (39.2%)</td>
<td>20085 (29.4%)</td>
</tr>
<tr>
<td>outpatient</td>
<td>17576 (60.8%)</td>
<td>48246 (70.6%)</td>
</tr>
</tbody>
</table>

As your comment, we classified prescription sources from outpatient setting or during admission period in Table1. It was the strongest associated factor in utilization of evidence based treatments, so we adjusted this factor in table 2, and 3.

Methods:

2. About study population, the primary diagnosis of heart failure was referring to admission diagnosis to the hospital or discharge diagnosis from the hospital?

In my opinion if the Authors are evaluating treatment after the hospitalization then they should consider the discharge diagnosis.
When patient used medical services, health care providers submit claims to the Korea’s Health Insurance Review Agency (KHIRA) for a review of the incurred medical costs. Therefore, KHIRA database is retrospective and diagnosis during admission is always confirmative diagnosis at discharge, So, our primary diagnosis of heart failure is discharge diagnosis. We also described it in methods part.

**Methods:**

3. About “covariates”, previous cardiovascular disease histories and other listed comorbidities have been adjusted in the logistic regression model? I think it should be elucidated.

We adjusted previous cardiovascular diseases in the logistic regression model. We described it more detail in statistical analysis and also presented in table 2 with multivariate logistic regression.

**Methods:**

4. Section “Utilization of evidence-based treatment in CHF elderly”:

   a. The first sentence presents mistakes: I think that percentage of patients is 71.4% not 70.3%. Furthermore the Authors should elucidate that they are referring to patients receiving “at least one drug” of the disease modifying treatments.

   We revised the above sentence according to your comment.

**Methods:**

4. Section “Utilization of evidence-based treatment in CHF elderly”:

   b. Joo Young et al describe the characteristic of the studied population, when comparing characteristic of different group they must report the statistical significance of their statements (p=…) and how they assess it (it could be added
For example, this statement needs to be confirmed by statistical analysis:

i. “The clinical characteristics of each treatment group were not different within the total study population.”

ii. “More patients in the A+B group had angina …. compared to those in the non-use group. However, dementia was more pronounced in the non-use group.”

iii. “Patients in the A+B group were more likely to receive … than were patients in the non-use group”

We appreciate your thorough review and compared each group of evidence-based treatments with the non-use group as control. We described our statistical analysis in the methods part and results part. We also showed our analysis in Table 1.

Methods: 5. Section “Predictive factors for the utilization of each evidence-based treatment”:

a. Throughout the test, the authors use the term “predictive factors”, however, taking into account that this is a cross-sectional study and the type of statistical analysis, this term cannot be used. Something like “factor associated with…” should be more appropriate.

We acknowledged our study was cross-sectional and changed “predictive factors” as “Factors associated with…” according to your comment.
treatment were dependent on heart failure severity…” Where is reported HF severity? How was it classified and assessed? The Authors should include this information in the text, and report the mean of heart failure severity in the tables. i. This is the same for the abstract, HF severity shouldn’t be listed in the factors associated with underutilization of EB treatment, unless the Authors reported date regarding it.

We agreed with your opinion. We deleted the comment of heart failure severity because we could not assess the severity of heart failure in our dataset.

**Methods:** 5. Section “Predictive factors for the utilization of each evidence-based treatment”:

c. Table 2 is never reported in the text. It should be useful for the reader to find it reported and better explained.

i. In Tab.2 total % of disease modifying group could be wrong (the sum of different group is 71.4% not 70.6%, as previously stated in this report)

We described table 2 and table3 in section of “Factors associated with the utilization of each evidence based treatment”. We also corrected the total % of disease modifying group as your comment.

**Methods:** 5. Section “Predictive factors for the utilization of each evidence-based treatment”:

d. Third paragraph (A+B group), to which table are the Authors referring to? It should be clarified. If Authors are referring to table 2 I think it could be interesting to underline the 0.83 O.R. for presence of chronic lung disease.
We referred to A+B group in table 2, and added the association of chronic lung disease and beta-blocker treatment. We added the above finding in the text.

Discussion

6. Third paragraph, “…Therefore, it could be inferred that the non-use group was more likely to be institutionalized”.

In my opinion the non-use group, that is associated with residence in rural area, is more probable to been admitted to smaller hospital (not tertiary) and treated by less specialized healthcare providers, thus receiving less updated treatments. I don’t understand how the Authors can inferred that this group was more likely to be institutionalized.

Thank you for your comment. In fact, we put a prescription source variable as your previous comment, and found that rate of prescriptions from outpatient setting in non use group was 54%. On the other hand, rate of prescriptions from outpatient setting in evidence based treatment group was 76.2%. So we could infer that a lot of patients with no use group were institutionalized. We add this comment in discussion part.

Discussion

7. Fourth paragraph, “Beta-blockers have been avoided due to a fear of aggravating chronic obstructive pulmonary disease and diabetic control.”

The Authors should modify this sentence. Indeed from this study there are not available data on aggravating of chronic obstructive lung disease or diabetic control. If these data are available, the Authors need to report them in the results. Otherwise they could only discuss the negative association between B-blockers use and presence of chronic lung disease and diabetes.
Thank you for your comment. What we tried to suggest was that many physicians have traditionally avoided the use of beta-blockers for fear of aggravating COPD or worsening glucose control in diabetes despite the adequate evidence of safeties. We revised the sentences in the text as follows: **Beta-blockers have been traditionally misunderstood as aggravating chronic obstructive pulmonary disease or poor glycemic control in diabetes.**

**Discussion**

8. When comparing to prescription rate of Gislason et al paper, the Authors made some little mistakes (the reported data are different from the data reported in the original paper of Gislason et al).

Sorry, I found mistakes. I revised the data from paper of Gislason et al.

**Minor revision: Methods:**

9. Add Standard Deviation when talking about mean age (second paragraph)

We added Standard Deviation of mean age as your comment.

**Minor revision: Methods:**

10. Third paragraph of Background: the first two sentences need references.

We added references as your comment.

**Minor revision: Methods:**

11. Third paragraph, at the end of first sentences “… and a residence was a rural area”. To this reviewer this sentences is not clear.

Wehouse of evidence based treatment group were more likely living in rural area.

We modified this sentence as above.
Minor revision: Methods:

12. Reading Methods “Data source” it seems that the Authors use diagnosis that has been coded in accordance with ICD10, however in the discussions the Authors report that the diagnosis of HF in the Khira database is not validated but compared to ICD10. This could be reported in Methods.

We put a statement in Methods part that diagnostic validity using ICD10 code was not validated.

Minor revision: Methods:

13. Study limitation: it is possible that some of the under-utilization of b-blockers reflects the fact that the patients had recently been hospitalized. It was generally recommended to stabilize patients first before initiating b-blockers.

We agreed with the reviewer’s opinion, and added the comment in discussion part.
Methods:

2. Are the methods appropriate and well described?

The methods are described with little detail. The authors consider the study as retrospective however; apparently this is a cross-sectional study employing back data. In this way, all analysis should take into account this aspect, as for example, in the choice of measure of association, where the authors employed the Odds Ratio with its respective 95% Confidence Interval as estimator, when in cross-sectional studies, the appropriate effect measure is the Prevalence Ratio (PR) with your 95%CI. The Odds Ratio tends to overestimate associations when compared to the PR, therefore, some of the variables could not show associated with the outcome being studied.

We appreciate your thorough review and accepted the reviewer’s comment. We changed the Odds Ratio to Prevalent Ratio with 95% CI. We described it in methods and showed at table 2 and table3.

Methods:

3. Are the data sound?

Despite having found significant associations (such as protective factors or risk factors) between virtually all variables when multivariate analysis was carried out, such findings cannot be considered reliable, considering that was analyzed a sample of large size, and may be introducing a error due to sampling effects, facts that may be suggested when observing the low magnitude of associations and the small size of the 95%CI. Therefore the results should be interpreted with
great caution and with very critical sense.

Database from the Korean Health Insurance Review and Assessment Service database (KHIRA) contains medical claims data for the entire Korean population as a result of the National Insurance Health System. Our data contains an elderly population admitted to hospital for heart failure in Korea. So it is not likely that specific population could be sampled and detected in KHIRA database. Still several limitations of our database exists. One is lack of validity in diagnosing heart failure by ICD-10 codes in KHIRA database. Another limitation is that this was cross sectional study using retrospective database so terms using risk factor or protective factor might be wrong. We changed the above terms to “associated factors”.

Discussion:

5. Are the discussion and conclusions well balanced and adequately supported by the data?

No, clearly the discussion was held only on variables that were “able” to predict the treatment prescription not based on evidence, in this way, the authors have lost the great opportunity of delving into the discussion of findings related to variables that behaved as protective factors, so the conclusions also were damaged.

We agreed to your opinion and this was cross sectional study using retrospective database. We tried to describe associated factors of evidence based treatment not predictive or risk factors in explaining the results.

Discussion:

6. Are limitations of the work clearly stated?

The authors cite three major limitations of the research, however, did not
comment on other important limitations, such as the use of a specific database linked to health insurance, which certainly also has a specific population can be lead to a selection bias. Similarly, database information do not provide guarantee of prior information of patients.

Another limitation, the database is relatively old (2005-2006), it is possible that after 5 to 6 years the situation is different, and the results cannot be extrapolated, impacting negatively on the external and internal validities of the study.

Another limitation of the sample corresponds to a large database (28,992 elderly), and statistically it is known that this can lead to the meeting of associations which on many occasions can be due exclusively to the sampling effect.

Database from the Korean Health Insurance Review and Assessment Service database (KHIRA) contains medical claims data for the entire Korean population as a result of the National Insurance Health System. Our data contains all elderly population admitted to hospital for heart failure in Korea. So it is not likely that specific population could be sampled and detected in KHIRA database. We accepted the fact that database information do not provide guarantee of prior information of patients and added it in limitation.

Thank you for your thorough comments. We added the study flow diagram in figure 1.

8. Do the title and abstract accurately convey what has been found?

In this topic, the methodology is described in some (few) detail and the results describe only associations of risk. There is no mention on other associations found (protective, for example).

The keywords do not meet formal descriptors (must be rewritten according to the MeSH)
We revised the methods with more detail and described factors associated with utilization of evidence based treatment in heart failure in results. We revised the keywords as MeSH terms. Thank you for your comment.

**Major compulsory revision:**

The statistical analysis should be rewritten with more details of techniques employed, leaving clear what factors or tuning variables were used?

We revised the statistical analysis with more detail as follows according to your comment,

We evaluated baseline characteristics with previous cardiovascular disease, medications and other systemic medical histories between each group of evidence based treatment and non use group using Student’s t test for continuous variable and chi-square test for categorical variables. Multivariable logistical regression model was used to evaluate clinical factors associated with each evidence based group. The model incorporated the following demographic factors (age, gender, residence area, utilization of hospital type, specialty of health care providers and type of prescription resources), previous cardiovascular diseases (angina, myocardial infarction, valvular heart disease, atrial fibrillation or flutter, transient ischemic attack), systemic medical diseases (hypertension, hyperlipidemia, chronic lung disease, end stage renal disease) and concomitant medications (heart failure medication, antidiabetic drugs) by one by one forward selection methods. We also performed the similar multivariable logistic regression analysis in subgroup who were treated with both digoxin and diuretics, which could indicate patients with symptom relieving treatment for heart failure. Subgroup analysis were shown for the purpose of increasing diagnostic accuracy for heart failure.
**Major compulsory revision:**

In the results should be described and properly interpret any Association found (risk and protective factors) according to multivariate analysis.

According to your comment, we revised the result of data with correction in table 2 and table 3. We added a variable regarding the sources of prescription from inpatient or outpatient. We used “Factors associated with” instead of “protective factor”. We described the factors associated with utilization of each evidence based treatment group more detail in results part.

**Minor compulsory revision:**

To use “MeSH” for choose of key-words.

We chose MeSH term for key words as your comment.