Author's response to reviews

Title: The impact of prior outpatient ACE inhibitor use on 30-day mortality for patients hospitalized with community-acquired pneumonia

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Author's response to reviews: see over
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Re: The impact of prior outpatient ACE inhibitor use on 30-day mortality for patients hospitalized with community-acquired pneumonia

Dear Editor:

Thank you for your review of our above-referenced article. We have revised the paper in response to the comments to the editor.

In closing, on behalf of the co-authors of this paper, I want to thank you for the review of our work. I believe that the article has improved based on the peer-review process. We hope that you deem the revised version suitable for publication in the BMC Pulmonary Medicine.

Sincerely yours,

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1) This is a study of association and therefore the strongest statements should be that clinical trials are warranted and no increase use of ACE inhibitors other than for established reasons are warranted.

We agree with the reviewer and have revised the discussion section accordingly (page 6, paragraph 2).

2) It is not clear how the definition of community-acquired pneumonia was made. How was nosocomial pneumonia and post-operative pneumonia removed? Were transfers from other hospitals excluded as nosocomial pneumonias?

For this study we used the standard criteria developed as part of the Pneumonia Patient Outcomes Research Team (PORT) study and subsequently utilized by Medicare in the community-acquired pneumonia quality improvement initiatives. [1, 2] To be included in this study patients must have:

1) Discharge ICD-9 criteria for community-acquired pneumonia.
2) Have a diagnosis of pneumonia on presentation to the hospital documented in the medical record.
3) Have a chest x-ray with findings consistent with pneumonia.
4) Not been transferred from another acute care hospital.

We are confident that this definition excludes hospital-acquired pneumonia. This criteria is listed in the Study Sites/Inclusion and Exclusion Criteria.

3) Death follow up was likely incomplete. Was death determination biased between groups?

We believe that the methods that we used to ascertain death are as close to the “gold standard” of the National Death Index as possible.[3, 4] Previous studies have demonstrated that the VA death files are 90 to 95% sensitive for mortality.[5-7] In addition, the mortality information from the Texas Department of Health is the source of the information from Texas that is input into the National Death Index.[8] Thus we find it unlikely that there was significant bias in the ascertainment of mortality.

4) Was use of ACE biased? Those most likely to live were most likely to be able to purchase drugs? The effect of ACE may have been confounded by the ability to purchase.

For the portion of our population that was hospitalized at the VA hospital medications are either free, or for those with incomes significantly above the poverty line require a small co-pay (currently $7 dollars a month). Comparing the use of ACE inhibitors we did find a significant difference in the use of ACE inhibitor use between the two hospitals (16.7% versus 30.3%). Therefore this is a limitation of our research. We have added this limitation to the discussion section (last paragraph page 5). However we do not feel that this significantly biases our paper. We repeated our multivariable analysis, stratifying by hospital, and found that there were the odds ratio were similar however there was greater variation in the confidence interval in the impact of ACE inhibitor use by hospital (hospital 1 OR 0.48, 95% CI 0.14-1.1 versus hospital 2 OR 0.44, 95% CI 0.18-0.94). Therefore we feel confident that our results are valid.
5) The use the propensity score could have been based upon
   a. Use of drug and adding score to the regression with double entry of the some covariates.
   b. The risk of death could have been modeled by propensity score of all covariates. The cases could have been matched by propensity score and a pseudo randomized trial reported with matching of cases by propensity score. The latter is a more powerful method to devise the study.

Regarding point (a) we specifically excluded all covariates that were in the propensity score from the final logistic regression model so there was no double entry in the model. Regarding (b) we have revised our multivariable analysis to use conditional logistic regression with matching on the propensity score. The results did not change significantly. The methods (page 4, paragraph 3) and results (page 5, paragraph 2) section have been revised accordingly.

6) Only 50% of those with a pneumonia received antibiotics in the first 24 hours. Either care was quite poor or the admission dx and discharge dx were often dissimilar. This fact question the dx of pneumonia to that of other disease (heart failure?) where the use of ACE would be known and useful.

Actually 100% of the cohort received antibiotics within the first 24 hours. Only 28% received antibiotics within 4 hours and an additional 22% of patients received antibiotics within 8 hours. The rest of the cohort (50%) received their initial dose of antibiotics within 24 hours. Although far from perfect these percentages are similar to what has been found in other studies.[9]

Referring again to comment #2 we are quite confident in the diagnosis of community-acquired pneumonia since we used accepted criteria for the diagnosis of community-acquired pneumonia in retrospective cohort studies. Therefore we do not feel that the study has been contaminated by other diagnoses that may confound our analysis. That being said we are unable to completely rule out that demonstrated effect may be due to quality of care issues. However we find it unlikely that a large number of patients had congestive heart failure, hypertension, or renal disease, and were not treated with ACE inhibitors. Therefore we do not feel that our study is biased in this manner.

References


