

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Impact of frailty on 30-day and 1-year mortality in hospitalized elderly patients with community-acquired pneumonia: a prospective observational study
AUTHORS	Luo, Jia; Tang, Wen; Ying, Sun; Jiang, Chunyan

VERSION 1 – REVIEW

REVIEWER	Zaher S. Azzam MD, FESC, Clinical Professor Department of Internal Medicine "B", Rambam Health Care Campus, Haifa, Israel Rappaport Faculty of Medicine, Technion, Haifa, Israel
REVIEW RETURNED	07-Apr-2020

GENERAL COMMENTS	<p>The investigators conducted this to examine the impact of frailty on short- and long-term mortality among elderly patients with community-acquired pneumonia (CAP). They concluded that frail patients are prone to develop severe CAP, and frailty is strongly related to prognosis of 1-year mortality. The investigators recommend frailty as a routine clinical practice and post discharge management. This study provides a simple prognostic tool in patients with CAP.</p> <p>Comments</p> <ol style="list-style-type: none">1. Page 5, lines 17-22. It is important to cite a reference regarding mortality from CAP in China. the incidence seems by far less than the reported in the US.2. In pneumonia, we have Pneumonia Severity scores such as CURB-65 and PSI. It is interesting to compare Frailty with see whether, frailty index will have advantage over PSI or CURB-65 scores.3. Although Severe community acquired pneumonia (SCAP) itself is implicated with poor prognosis; HR was 52 which is higher than frailty which was 2.84. Thus it seems that the added value of frailty in case of SCAP is minor.
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REVIEWER	Mark Q Thompson University of Adelaide, Australia
REVIEW RETURNED	08-May-2020

GENERAL COMMENTS	Thank you for the opportunity to review this manuscript. This study of 256 older adults hospitalised due to CAP found that frailty was common, frail patients were more likely to experience SCAP a had higher 1-year mortality rate compared with non-frail patients. This
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	<p>is an interesting study that has clinical implications for the management of patients hospitalised with these conditions in combination. Statistical approach was appropriate. A number of points requiring attention are highlighted below. Other comments can be found throughout the pdf.</p> <p>Major Points:</p> <p>1) I would recommend only reporting adjusted / multivariable analysis, but keep unadjusted results in tables.</p> <p>2) You can't attribute frailty causation to SCAP (I have highlighted these instances in the manuscript text) as cross sectional analysis at baseline. You only can report association for this, but can rightly describe prediction for frailty, etc and mortality.</p> <p>3) A key finding which you haven't reported is the association between frailty and CAP admission. This is an obvious important feature of your study, which is currently missing. You have reported frailty n(%).</p> <p>4) An additional analysis in terms of examining survival HRs might be to stratify as follows:</p> <ul style="list-style-type: none"> - non-frail CAP - non-frail SCAP - frail CAP - frail SCAP <p>This would offer an interesting comparison of each of these categories with implications for clinical management. Do the frail with SCAP have worse mortality outcomes in comparison to the non-frail with SCAP?</p> <p>5) The discussion section has a number of paragraphs which don't tie together your findings to the literature.</p> <p>6) Your key messages need to be emphasised throughout this paper:</p> <ul style="list-style-type: none"> - older adults admitted due to CAP were (i am assuming, but you have not reported or stated this) significantly more likely to be frail - frail individuals are significantly more likely to present with severe CAP - 1-year mortality is significantly higher for frail individuals hospitalised with CAP, compared to non-frail. <p>- The reviewer provided a marked copy with additional comments. Please contact the publisher for full details.</p>
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VERSION 1 – AUTHOR RESPONSE

The impact of frailty on 30-day and 1-year mortality in hospitalized elderly patients with community-acquired pneumonia: a prospective observational study

- We found the reviewer's comments most helpful and have revised the manuscript. The title has been changed to "The impact of frailty on 30-day and 1-year mortality in hospitalized elderly patients with community-acquired pneumonia: a prospective observational study".

Conclusions: The current findings suggest that frailty is strongly associated with severe CAP and higher 1-year mortality in elderly CAP patients, and it should be considered in the management of CAP in elderly patients.

- Thank you very much for your comments and suggestions. I have rectified the narrative of the conclusions according to the Reviewer's comments.

Community-acquired pneumonia (CAP) is the leading cause of infectious disease in the elderly and is associated with high rates of mortality, morbidity, and high costs worldwide.[1, 2, 3, 4] In the United States, the incidence of CAP in adults between 65 and 79 years old is 63 cases per 10,000 adults and increases to 164.3 cases per 10,000 adults in the over-80 age group.[5] In China, the reported mortality due to pneumonia is 23.55 cases per 100,000 adults aged between 65 and 69 years old and nearly 36 times greater in persons over 85 years.[6]

- Thanks for the advice. I have added the reference in the original sentence. Specific data is provided by reference 6.

Refer to website: [http:// www.nhfpc.gov.cn/htmlfiles/zwgkzt/ptjnj/year2013 / index2013.html](http://www.nhfpc.gov.cn/htmlfiles/zwgkzt/ptjnj/year2013/index2013.html).

Well-known risk factors for mortality, such as age, functional status, comorbidities, and others, have already been incorporated into the assessment of the severity of CAP,[4,6,7,8,9,10] but increasing mortality in elderly CAP patients indicates the need for the identification of novel, ideally modifiable, risk factors for poor outcomes. Particular attention has recently been directed to the concept of the "frail elderly patient". Although frailty has been considered synonymous with disability, comorbidity, or advanced old age, it is defined as a cumulative decline and loss of physiological reserves in multiple organs and systems and causes increased vulnerability to adverse outcomes, including falls, hospitalization, and mortality.[11,12,13] Moreover, frailty has been confirmed to be an independent risk factor for mortality in patients with acute and chronic diseases.[14,15] A European multicenter study that included 5021 patients assessed the impact of frailty on intensive care unit (ICU) admission and 30-day mortality in elderly patients. The results indicated that frailty (measured by the Clinical Frailty Scale) was found in 43% of patients and was independently related to 30-day survival (hazard ratio (HR) 1.54; 95% confidence interval (CI) 1.38-1.73 for frail versus non-frail patients).[16] The few reported studies focused on frailty and CAP have indicated that frailty factors contributed to increasing post-CAP hospitalizations,[17] and frailty significantly predicted 1-month mortality in older patients.[18] Therefore, we hypothesized that frailty was related to the prognosis of CAP, especially the presence of frailty was associated with negative predictive value in elderly CAP patients (in terms of CAP prognosis and mortality).

- Thanks for the reviewer's suggestion . I have added reference 4 and 6 to prove that the assessment of the severity of pneumonia requires consideration of age and comorbidities. Widely used assessment method such as CURB-65 or PSI also included the items about it.

- Thanks for the reviewer's suggestion. I have checked the inappropriately cited reference and deleted it.

- Thanks for the reviewer's kind advice. According to the advice, I have modified the logic of the language and made targeted change.

- Thanks for the reviewer's kind advice. I have changed the reference.

- Thanks for the reviewer's kind advice. According to the advice, I have deleted the original sentence and described the information provided in the literature in detail.

- Thanks for the reviewer's kind advice. I have made correction according to the Reviewer's comments.

- Thanks for the reviewer's kind advice. I have changed the original sentence.

Frailty was assessed by the Frailty Phenotype (FP): unintentional weight loss, self-reported exhaustion, weakness, slow gait speed, and low physical activity.[20] Each construct is assigned "1" if present or "0" if absent. The FP ranges from 0–5; consistent with established definitions, in this study we defined frailty as the FP score of ≥ 3 , non-frail as the FP score of 0-2.

- Thanks for the reviewer's kind advice. "FFP" was incorrectly stated in the original manuscript. This has been rectified. The authors are grateful to the referees for pointing out their error.

- Thanks for the reviewer's kind advice. My previous description is unclear, and I have modified the sentence. I measured frailty using the original criteria and cut-points specified by Fried.

Functional status assessments were carried out with the Barthel Index (BI) to evaluate the activities of daily living.[4722]

- Thanks for the reviewer's kind advice. I have added the reference in the original manuscript. According to the BI original paper, we used the values in an ordinal scale, not modified scale.

The nutritional status assessment was conducted with the unified Mini Nutritional Assessment-Short Form (MNA-SF) questionnaire.[23] The questionnaire consists of BMI, weight loss in the past 3 months, dietary changes, stress or acute illness, activity, and neuropsychiatric diseases. The total score is 14 points. Scores of 0-7 indicated malnutrition.

- Thanks for the reviewer's kind advice. I have changed the original sentence and modified the standard in the baseline assessment.

All patients were followed for 1 year after admission. Deaths were confirmed through surveillance or matched to official death records. The primary outcomes were all-cause mortality at 30 days and 1 year after admission to the hospital.

- Thanks for the reviewer's kind advice. A total of 256 patients completed the followed-up for 1 year after admission. There was a detailed description in the following results. Deaths were confirmed through surveillance or matched to official death records. I have modified the description in the original sentence.

Patients or the public did not involve in the design of the study, recruitment or conduction of the study. There are no plans to involve participants in dissemination of results. The results of the study would be disseminated to patients once he or she requests so and aggregated data would be reported in project reports and research publications and conferences.

- Thanks for the reviewer's kind advice. According to the magazine requirements, we have made correction according to the Reviewer's comments. Results

In total, 393 patients with CAP were admitted to our department during the study period, 119 patients with the concomitant diseases before admission were excluded (Figure.1), and 18 were excluded due to loss to follow-up. A total of 256 patients (range, 65-99 years) were included for the final statistical analysis. Demographic patient characteristics are presented in Table 1. Median (IQR) population age was 86 (81, 90) with 180 (70.3%) males. The frail and malnutrition status were reported in 171

(66.8%) and 71 (27.7%), respectively. Fifty-seven (22.3%) of the patients had SCAP. All-cause mortality for the 256 patients with CAP was 5.5% at 30 days and 16.8% at 1 year.

In the analysis 85 (33.2%) non-frail subjects were compared to the frail group of 171 (66.8%) patients. Frailty was significantly associated with older age, female, lower BMI, worse activity ability of daily living function, comorbidity, and poorer nutritional status. The proportion of SCAP in the frail group is higher (28.65% vs 9.41%, $P < 0.001$), and frail patients experienced higher 30-day mortality ($P = 0.015$) and 1-year mortality ($P < 0.001$). The results of Cox proportional hazards regression are presented in Table 2 and Table 3. Several variables were significantly associated with 30-day mortality in univariate, including SCAP, frailty, malnutrition, CCI. In a multivariate analysis (Table 2) only SCAP (multivariate-adjusted HR 30.60, 95% CI 3.77-248.06) remained significant. To determine the significant risk factors for 1-year mortality in patients with CAP (Table 3), in a multivariate analysis, SCAP (adjusted HR 7.68; 95% CI: 3.79-15.58), frailty (adjusted HR 2.70, 95% CI 1.69-4.39), and CCI (adjusted HR 1.19, 95% CI 1.05-1.34) were independent risk factors for 1-year mortality.

Furthermore, we conducted a subgroup analysis only enrolled severe CAP patients. In all SCAP subjects ($n = 57$), eight patients (14%) were non-frail and forty-nine patients (86%) were frail. The frail group with SCAP reported worse activity ability of daily living function and nutritional status, higher 30-day and 1-year mortality (Table 4). Several variables were significantly associated with 1-year mortality of SCAP in univariate, including frailty, malnutrition, function status, CCI. In a multivariate analysis (Table 5) only frailty (adjusted HR 2.87, 95% CI 1.58-4.96) and CCI (adjusted HR 1.16, 95% CI 1.01-1.34) remained significant. There was no significant risk factor correlated with the 30-day mortality after the multivariate analysis.

- Thanks for reviewer's constructive comments. I have merged table1 and table 2 in original paragraph. I still have modified the description in the later paragraph. In addition, I have conducted a subgroup analysis of severe pneumonia patients in the later period, and I have get interesting results.

The key points of this study are as follows: 1. Our study identified that frail CAP patients were significantly more likely to present with severe pneumonia and had significantly increased 30-day and 1-year mortality; 2. Frailty was an independent risk factor correlated with 1-year mortality even after adjustment for age, sex, disability, malnutrition, comorbidities, and severity of CAP, but it was not the independent risk factor for the 30-day mortality.

- Thanks for the reviewer's kind advice. I have rectified the incorrectly narrative in the original paragraph.

The incidence of CAP increases with increasing age and results in higher risks of morbidity and mortality. Mortality in elderly patients with CAP maybe 25% higher than in the general population (10%).[4,9] Our study demonstrated that all-cause mortality for elderly patients with CAP was 5.5% at 30 days and 16.8% at 1 year. Different independent prognostic factors related to mortality have been well described, including age, comorbidities, functional status, microbial etiology, and early ad-equate antibiotic treatment.[9,10,24,25] Recently, most authors noted that in the elderly population, age per se is not an independent predictor of mortality.[26,27] Interestingly, We found that all patients who died were in the frail-group, whether in 30-day or 1-year followed-up. Although frailty is considered to be synonymous with disability, comorbidity, or advanced age, Fried LP et al defined it as a complex age-related clinical condition characterized by a decline in physiological capacity across several organ systems, with a resultant increased susceptibility to stressors.[20,28,29] This vulnerability results in an increased risk of adverse health outcomes including falls, disability, hospitalization, institutionalization, and death. Various conditions, including malnutrition, sarcopenia, gait impairment, chronic inflammation, polypharmacy, cardiovascular changes, and morbidity, were found to be associated with and potential causes of frailty. [30,31,32]

- Thanks for the reviewer's kind advice. I have added the description of mortality in elderly CAP patients and relevance to this article.

- Thanks for the reviewer's kind advice. I have modified the description in the original paragraph. I would like to indicated that although age and comorbidity have been validated for pneumonia severity assessment and prognosis, but maybe frailty would be a more ideal component choice for assessing the severity in elder patients.

- Thanks for the reviewer's kind advice. I have modified the description in the original paragraph.

However, in our study, there was no significant association between the nutrition status and 30 day or 1-year mortality after multivariate analysis (adjust-HR 1.11, 95% CI 0.90-1.35; adjust-HR 0.94, 95% CI 0.81-1.10, respectively). Recent studies have shown that frailty and malnutrition are intrinsically interrelated in terms of structure, identification tools, and treatment.[30,32,35] Malnutrition is also an important biological mechanism underlying the occurrence and development of frailty.[31] In our study, frailty was defined by the Fried Phenotype criterion, in which not only got unintentional weight loss as a criterion but also included functional status such as slow gate speed and low levels of physical activity. This may explain why frailty, but not malnutrition and disability, was significantly associated with higher mortality in multivariate analysis.

Our study also confirmed that frailty was very common in elderly patients with CAP (the prevalence was 66.8%) and significantly associated with the severity of the disease, for 1-year, frailty HR of 2.70 is nearly triple the mortality of non-frail.

- Thanks for the reviewer's kind advice. I have modified the description and trimmed down the discussion in the original paragraph.

The results of the study demonstrated that frailty was independently associated with 1-year mortality after adjusting for the variables mentioned earlier, which implies that frailty can effectively predict the adverse outcomes.

- Thanks for the reviewer's kind advice. I have rectified the incorrectly narrative in the original paragraph.

VERSION 2 – REVIEW

REVIEWER	Mark Q Thompson University of Adelaide
REVIEW RETURNED	26-Jun-2020

GENERAL COMMENTS	<p>Thank you for re-submitting this paper and for offering me the opportunity to review. The revisions have improved the paper, however, there are a number of issues which require attention. These are detailed below and in the marked-up pdf.</p> <p>Major Points</p> <p>Inflammatory biomarkers (p14, para 2) These is a large paragraph in the discussion on biomarkers of infection which only briefly mentions your findings (hs-CRP and PCT findings). Most of this discussion is regarding findings from studies without much connection to your study. This is the first time biomarker findings are reported in the paper (other than</p>
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	<p>Table 1 results). You have listed them as variables in the baseline assessment, however, there is no commentary in the introduction, or findings in the results section. Why are the two biomarkers above mentioned in discussion and not the others listed in Table 1?</p> <p>Report in a standard way throughout the manuscript for biomarkers as you would for any other associated factors. It might be useful in the discussion to describe the concept of infection biomarkers together with biomarkers frailty. Consider how much attention you wish to apply to this topic in the manuscript. I suggest adding a reviewer with expertise in this field to review the manuscript.</p> <p>Hazard Ratios - Subgroup analysis (p11, para 2) Keep the focus of mortality reporting on adjusted HRs. What I want to read here are the adjusted HRs (3-month and 1-year) for this subgroup. Table 5 is useful but the 3-month equivalent table is missing (merge these tables together). Then make sure to be clear in reporting who is at risk. E.g., For patients admitted with severe CAP, those who were frail had nearly triple the 1-year mortality risk (HR 2.87, etc) compared with those who were non-frail. I recommend moving Table 4 to supplementary table. Exclude the commentary about unadjusted factors associated with mortality.</p> <p>Minor Points</p> <p>Please see comments in the pdf</p> <p>Communicating Findings There are a number of instances throughout the manuscript where the meaning of sentences is unclear. English language editing is recommended.</p>
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VERSION 2 – AUTHOR RESPONSE

Replies to Reviewer 1

We apologize for not providing point-to-point responses in the first reply letter and appreciate your considerations and insightful comments. The changes in the text and responses to the comments are provided below:

Specific Comments

1. Page 5, lines 17-22. It is important to cite a reference regarding mortality from CAP in China. the incidence seems by far less than the reported in the US.

Response: Thank you for the suggestion. Several sentences were changed in the Discussion section (Page 4, Lines 6-7).

We added the following reference: Cao B, Huang Y, She DY, et al. Diagnosis and treatment of community-acquired pneumonia in adults: 2016 clinical practice guidelines by the Chinese Thoracic Society, Chinese Medical Association. Clin Respir J. 2018;12(4):1320-60.)

One study reported the incidence of CAP by age group but not in the total adult population in China, and no studies estimated mortality from CAP in the Chinese population. In 2012, the average mortality from pneumonia in the overall population was 17.46/100 000 in China, 23.55/100 000 in the population aged 65–69 years, and $\leq 864.17/100\ 000$ in the population aged >85 years.

2. In pneumonia, we have Pneumonia Severity scores such as CURB-65 and PSI. It is interesting to compare Frailty with see whether, frailty index will have advantage over PSI or CURB-65 scores.

Response: Thank you for the thoughtful suggestion. We initially collected CURB-65 data, and compared them to frailty, and analyzed discriminatory performance by the receiver operating characteristic curve. However, sampling bias (CURB-65 scores ≥ 2) has been reported. For this reason, we did not list the data in the final results. Moreover, given that our cohort included hospitalized elderly patients with CAP, we selected the IDSA/ATS 2007 criteria to define the severity of pneumonia and conducted subgroup analysis to evaluate the association between frailty and SCAP. We were unable to perform a stratified analysis of pneumonia severity using PSI because not all PSI parameters were included in the study design. Nonetheless, we agree that future studies should include outpatient and inpatient CAP patients in the experimental design and analyze the correlation between CURB-65, PSI, and frailty.

3. Although Severe community acquired pneumonia (SCAP) itself is implicated with poor prognosis; HR was 52 which is higher than frailty which was 2.84. Thus, it seems that the added value of frailty in case of SCAP is minor.

Our results confirmed that the severity of pneumonia has a significant impact on the short- and long-term prognosis of elderly patients with CAP. However, the incidence of severe pneumonia was higher in frail patients. Moreover, in subgroup analysis, 1-year mortality risk was nearly three-fold higher in frail patients with CAP (adjusted HR, 2.87; 95% CI, 1.58-4.96) than in non-frail patients. Therefore, we consider that frailty has high clinical value for patients with CAP, especially for predicting 1-year mortality.

Replies to Reviewer 2

Major comments:

1. Inflammatory biomarkers (p14, para 2)

These is a large paragraph in the discussion on biomarkers of infection which only briefly mentions your findings (hs-CRP and PCT findings). Most of this discussion is regarding findings from studies without much connection to your study. This is the first time biomarker findings are reported in the paper (other than Table1 results). You have listed them as variables in the baseline assessment,

however, there is no commentary in the introduction, or findings in the results section. Why are the two biomarkers above mentioned in discussion and not the others listed in Table 1?

Report in a standard way throughout the manuscript for biomarkers as you would for any other associated factors.

It might be useful in the discussion to describe the concept of infection biomarkers together with biomarkers frailty.

Consider how much attention you wish to apply to this topic in the manuscript. I suggest adding a reviewer with expertise in this field to review the manuscript.

Response: We appreciate these considerations and insightful comments. We initially included the analysis of the association between inflammatory markers and frailty. Because we were interested in the results that compare to frailty, inflammatory markers did not contribute significantly to the prediction of mortality after multivariate analysis. In our cohort, there was no significant correlation between CAP, frailty, and inflammatory markers. Thank you very much for the suggestions put forward by the editor in the revised opinion. Because our research results alone cannot draw any conclusions on the indicators of frailty, inflammation and the prognosis of CAP, our team decided to delete this part of the relevant discussion content in the original text after careful discussion. Thank you very much!

2. Hazard Ratios - Subgroup analysis (p11, para 2)

Keep the focus of mortality reporting on adjusted HRs.

What I want to read here are the adjusted HRs (3-month and 1-year) for this subgroup. Table 5 is useful but the 3-month equivalent table is missing (merge these tables together).

Then make sure to be clear in reporting who is at risk. E.g., For patients admitted with severe CAP, those who were frail had nearly triple the 1-year mortality risk (HR 2.87, etc) compared with those who were non-frail.

I recommend moving Table 4 to supplementary table. Exclude the commentary about unadjusted factors associated with mortality.

Response: Thank you for the helpful comments. We improved the description to focus on adjusted HRs. We transferred the data from Table 4 to a Supplementary Table and excluded the sentence on unadjusted factors associated with mortality. Only CCI was correlated with 30-day mortality in subgroup analysis by frailty status, and none of the study variables were significantly correlated with 30-day mortality in the multivariate analysis. Therefore, data on the risk of 30-day mortality were described in the text but were not included in a separate table.

Significant risk factors for 30-day mortality in patients with severe community-acquired pneumonia in COX proportional hazards regression analyses (n=57).

	Univariate		
Variable	HR	95% CI	P-value

CCI	1.21	1.02–1.43	0.028
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Data are estimated hazard ratios and 95% confidence intervals of explanatory variables in the 30-day mortality group.

Abbreviations: HR, hazards ratio; CI, confidence interval; CCI, Charlson’s Comorbidity Index.

Minor points:

1. Page 3, lines 51. We discussed HRs and added subgroup data on 30-day mortality in results. However, these HR values were not included in the abstract because the association between frailty and 30-day mortality was not significant.
2. Page 4, lines 4. Thank you for the advice. The text was changed accordingly.
3. Page 5, lines 28. Thank you for the suggestion. The text was improved as follows: “Studies have shown that age, functional status, comorbidities, and malnutrition are important factors associated with poor prognosis in CAP patients,^[4,6,7,8,9,10] and higher mortality in elderly CAP patients indicates the need to identify novel, modifiable risk factors for poor outcomes.”
4. Page 8, lines 24. We appreciate the recommendation and improved the text.
5. Page 9, lines 4. The text was edited.
6. Page 10, lines 34. The text was improved.
7. Page 10, lines 43. This sentence was deleted.
8. Page 10, lines 51. The text was clarified.
9. Page 10, lines 53. The text was changed.
10. Page 11, lines 10. The description was improved.
11. Page 11, lines 20-26. The proposed changes were implemented in the text.
12. Page 13, lines 25. The necessary changes were made in the text.
13. Page 15, lines 40. A reference was added to the manuscript.
14. Page 26, lines 3. These tables were merged.

VERSION 3 – REVIEW

REVIEWER	Mark Q Thompson
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	University of Adelaide. Australia
REVIEW RETURNED	07-Aug-2020

GENERAL COMMENTS	<p>This article is a much better read now, more clearly communicates your findings, and also describes how the findings might have an influence on clinical practice. All of the major points raised previously have been addressed. There are only a few minor points for follow up. I have mentioned these below and have marked up the pdf with comments.</p> <p>Tables Please be consistent with variables included in mortality analysis. E.g., BI and BMI are not included in table 2 (30-day), BMI not in Table 3. For the SCAP subgroup, 30-day mortality findings are mentioned in results but are not in the table. Please include these in similar format to Table 2. Please add a * after significant findings in tables 2 and 3. Makes it easier for the reader to scan over tables.</p>
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VERSION 3 – AUTHOR RESPONSE

Replies to Reviewer 2

Response: We appreciate these considerations and insightful comments. Your careful revision made our article a great improvement. The text was changed accordingly. The table 2 and table 3 were improved. We showed all variables results in the tables, and add a * after significant findings.

VERSION 4 – REVIEW

REVIEWER	Mark Q Thompson University of Adelaide Australia
REVIEW RETURNED	28-Aug-2020

GENERAL COMMENTS	<p>All the points raised in previous feedback have been addressed, with the exception of one point: - Supplementary table heading. Should read: Characteristics of patients with severe community-acquired.... Two other minor points: Tables 2 and 3 headings: should read 'associated' instead of 'associate', and 'Cox' instead of 'COX'. These points can be changed without returning to me. I recommend accept for publication. This paper will make a valuable contribution to our understanding of the risk profile of frail older adults hospitalised with community acquired pneumonia.</p>
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VERSION 4 – AUTHOR RESPONSE

Thank you very much for the decision letter and advice on our manuscript (ID: bmjopen-2020-038370) titled "Impact of frailty on 30-day and 1-year mortality in hospitalized elderly patients with community-acquired pneumonia: a prospective observational study." We also thank the reviewers for further

reviewing the manuscript and addressed the inappropriateness. All amendments are indicated by red font in the revised manuscript. According to editorial request, we rectified the first two bullet points of the strengths and limitations section.