July 7, 2017

Lena M. Chen, MD, MS

University of Michigan

Division of General Medicine

North Campus Research Complex

2800 Plymouth Road

Building 16, Room 407E

Ann Arbor, MI 48109-2800

email: lenac@umich.edu

Andrew Auerbach, MD, MPH

Editor in Chief

Journal of Hospital Medicine

John Wiley & Sons, Inc.

111 River Street

Hoboken, NJ 07030

Re: Journal of Hospital Medicine - Decision on Manuscript ID JHM-17-0106

Dear Dr. Auerbach:

Thank you very much for inviting us to re-submit our manuscript – “Relationship between Hospital 30-Day Mortality Rates for Heart Failure and Patterns of Early Inpatient Comfort Care” – for consideration for publication in the Original Research section of *Journal of Hospital Medicine.*

We very much appreciate the comments and suggestions of all of the reviewers, and have addressed each reviewer’s questions in a point-by-point fashion. We believe that this process has strengthened the manuscript.

Thank you very much for considering our manuscript for publication. Please do not hesitate to contact me if any additional information would be helpful.

Sincerely,

Lena M. Chen, MD, MS

**Editor’s Comments**

**E1)** *Thank you for your interesting analysis, which may be of interest to our readers. As the reviewers point out, your metric of "early comfort care" (e.g., on day 0-1) is problematic. While we understand that the GWTG-HF dataset had limited response choices, it would still be worthwhile to further explore the distribution of the timing of comfort care.*

We appreciate your comment and explore the distribution of comfort care in our sample in the table below. The vast majority of patients, more than 90%, did not transition to comfort care any time during their hospital stay.

|  |  |
| --- | --- |
| Category | N (%) |
| Day 0-1 | 2621 (2.79%) |
| Day 2+ | 5038 (5.36%) |
| Timing Unclear | 661 (0.70%) |
| Not Documented | 85600 (91.14%) |

We apologize that we did not clearly explain why we used the metric “early comfort care,” defined as comfort care on day 0-1. We chose to examine early comfort care because we were interested in exploring whether or not hospitals that provide early comfort care – a form of high quality care in many instances -- are penalized by a more standard measure of quality: mortality rates. Comfort care at any time during the hospitalization is a noisier signal, since comfort care provided a day before a patient’s death is not high quality care if that patient’s death was predictable.

Furthermore, most hospitalized patients transition to comfort care before they die, if the death is in any way predictable. Thus, if comfort care is measured at any time during the hospitalization, hospitals that have high mortality rates will also have high comfort care rates. Indeed, we found a positive, statistically significant correlation (correlation=0.32, p<0.0001) between RSMRs and any comfort care (see also, figure below). But, because the any comfort care measure is imprecise, we think this association is unlikely to reflect high mortality rates – and unintended penalties -- at hospitals with early advanced care planning.

**Figure. Hospital-level association of risk-standardized mortality rates with comfort care rates, when comfort care is instituted at any time during hospitalization**



correlation = 0.320

p < 0.0001

In the revised text, we better explain why we chose to use early comfort care as one of our primary outcomes. We write:

We chose to examine early comfort care because many hospitalized patients transition to comfort care before they die, if the death is in any way predictable. Thus, if comfort care is measured at any time during the hospitalization, hospitals that have high mortality rates are likely to have high comfort care rates. Therefore, we chose to use the more precise measure of early comfort care.

**E2)** *Do you have information on length of hospital stay?*

 We added this information to Table 1B.



**E3)** *Figure 1 may be of more interest if stratified by the different categories of comfort care timing*

We appreciate the suggestion and agree that a stratified figure is more interesting. We have modified Figure 1 accordingly.

E**4)** *Figure 2: it is not clear what the units are for the y axis ("frequency"), please edit appropriately*

 We apologize for the poor labeling and have corrected this. The y axis is frequency, defined as number of sites.

**Reviewer #1:**

*A very nicely done, thorough study that examines important and under-explored questions about the rate of early comfort care for patients hospitalized for HF, how that rate has trended over time and whether RSMR varies based on hospitals' rate of early comfort care.*

**R1.1)** *I think it would be helpful to further describe why you chose to focus on the rate of early comfort care (hospital days 0-1) rather than comfort care at any point in the hospital. Both seem of interest and I'm not clear why you did not examine the latter.*

 We agree and apologize that we did not explain this in our original manuscript text. Please see the response to E1.

**R1.2)** *It would be helpful to include additional discussion to explain the somewhat discrepant findings that 1) Risk-standardized early CC rates were not correlated with RSMR but 2) hospitals with above average comfort care rate of comfort care did have a decrease in their mortality rate after CC adjustment and may be adversely profiled. Do you think this latter point should lead to further consideration/improvement of the RSMR calculation or process?*

We appreciate the reviewer’s comments. We believe our paradoxical finding -- that hospitals with an above average risk-adjusted comfort care rate did have a decrease in their risk-standardized mortality rate (RSMR) after adjustment for the risk-adjusted CC rate, even though overall there was no correlation between risk-standardized CC rates and RSMRs -- is not due to higher CC rates at those hospitals, but some other aspect of those hospitals and their patients (some unmeasured factor contributing to hospital variation in comfort care and mortality risks), which we are not capturing in our models. Because the change was so small (-0.07% change in mortality rate), we believe the more policy-relevant finding is that risk-standardized early CC rates had a small positive, but statistically insignificant, correlation with RSMRs. The strength and significance of this correlation may change if early CC rates increase over time.  We have modified our abstract and discussion to reflect this more nuanced interpretation of our findings.

**R1.3)** *Page 2 line 29: Please add "early" to the sentence "Hospitals' early comfort care rates..."*

We made this change.

**R1.4)** *Page 2 line 31: Would be nice to include the range in rates of early comfort care (x-y%) in the abstract, as this is a key finding of your work*

We agree and added the range of 0-40% to the abstract.

**R1.5)** *Page 2 line 49: Period after RSMR*

We corrected this typo.

**R1.6)** *Page 3, line 34: Would be helpful to include data about the rate of hospice care in patients with HF, or the trend in this rate over time. Also, it's worth noting that though more patients are using hospice, many patients are using it for a brief period of time (e.g. <3 days prior to death) so hospice use is not skyrocketing quite as your text suggests*

We appreciate the reviewers’ comments. We added text and references as suggested, and toned down our language on increasing use of hospice. We now state.

Over time, this therapeutic perspective has become more common, with use of hospice care doubling from 23% to 47% between 2000 and 2012, among Medicare beneficiaries who died. For a national cohort of older patients admitted with heart failure – not just those patients who died in that same year -- hospitals’ rates of referral to hospice are considerably lower, averaging 2.9% in 2010 in one study. Nevertheless, it is possible that hospitals that more faithfully follow their dying patients’ wishes and withdraw care at the end of life might be unfairly penalized, if such efforts resulted in higher mortality rates than other hospitals.

**R1.7)** *Page 3, line 36: Do not use the phrase "withdraw care" but rather "withdraw life-prolonging interventions" as there's always more "care" that can be provided even if the goal is comfort*

We agree that the suggested wording is more appropriate and have made the change in the revised text.

**R1.8)** *Page 4, line 51: "CMO" has not yet been defined in your manuscript so please define prior to using the abbreviation*

 We apologize for this oversight and made this change.

**R1.9)** *Statistical analyses section is very thorough, clear and helpful.*

 Thank you for your comment.

**R1.10)** *Page 6, line 38: Space after 3)*

We corrected this typo.

**R1.11)** *Page 8, line 43: I'm not entirely clear about how the 90 hospitals with CC rates above the median mortality decreased after CC adjustment and I wonder if this could be better explained or shown. This also needs to be discussed further in the discussion, as per my above critique.*

 Please see our response to R1.2. We also now explicitly state the following in our Discussion:

For those hospitals with high comfort care rates, adjusting for comfort care did lower mortality rates, but the change was so small as to be clinically insignificant.

**R1.12)** *Page 11, line 38: Your point about not having information about patient or family wishes regarding end-of-life care is a very important one and you might want to highlight it by putting it at the start of your limitations section and/or saying something about how further research could seek to rectify this issue.*

 We started the Limitations section with this limitation, and stated the importance of future research focused on understanding patients’ wishes regarding end-of-life care.

**R1.13)** *Page 12, line 8: Paragraph break before "In summary"*

We made this change.

**Reviewer #2**

*This is an observational study using the Get With the Guidelines registry to describe the epidemiology of use of early comfort care for hospitalized heart failure patients, and examine the effect of hospitals’ rates of initiation of comfort care on risk-standardized mortality rates (RSMR) for heart failure.  The authors found wide variation among hospitals in the rate of initiation of early comfort care, and no association between risk-adjusted early comfort care and RSMR.

This study adds a valuable contribution to our understanding of the kind of care that hospitalized heart failure patients receive at the end of life, and begins to address a possible limitation of the use of RSMR as a quality metric.  Enthusiasm was tempered by the following areas in need of further attention:*

**R2.1)** *One of the study’s main outcomes, “early comfort care,” was defined as initiation of comfort care on hospital day 0 or 1, and all other possible outcomes were described as “late/no comfort care,” though effectively in the analysis the authors considered the outcome as a yes/no binary outcome. This seems to be a function of the registry, but in reality, comfort care is often initiated a few or several days into a hospitalization, after a trial of therapy and goals of care conversations with patients and families.  Lumping comfort care on day 2 with no comfort care obscures a possible relationship between slightly later (and likely appropriate) use of comfort care and mortality rates, which would be interesting to know and relevant to the question of whether RSMR inappropriately penalizes hospitals that provide comfort care.  The imprecision of the current measure biases the analysis toward the result of no difference, which was what the authors found.

At the very least, this should be addressed in the discussion, and a clinical or quality-related justification for the choice of looking at “early comfort care initiation” defined as comfort care within first two days rather than “any comfort care” (or over a different time period) should be given.  If it is possible to redo the analysis considering any comfort care vs. no comfort care, it would be meaningful to rerun the RSMR/risk-adjusted comfort care correlation test to see if the relationship is significant.  A breakdown of the responses to the question about comfort care initiation would also help in clarifying this measure, as would any prior demonstration of its validity.*

 We apologize for not clarifying why we chose to focus on early comfort care. We make this clearer in the revision. We also re-ran the correlation test for RSMR/comfort care, and defining comfort care as any comfort care. We found a significant positive association. We suspect that this is because patients whose deaths are imminent are made comfort care at most institutions. Please also see our response to E1.

 With regards to the validity of the comfort care measure, the comfort care question in GWTG-HF is identical to the one used by CMS and The Joint Commission. <https://manual.jointcommission.org/releases/TJC2016A/DataElem0031.html>

An audit of the GWTG-stroke comfort care measure, which is nearly identical to that used in GWTG-HF, had 99.1% accuracy and an interrater reliability of 0.97 with a 95% CI of 0.93 to 1.00. (Reference: Xian Y. et al., Data quality in the American Heart Association Get With The Guidelines-Stroke (GWTG-Stroke): Results from a National Data Validation Audit. Am Heart J. 2012; 163: 392-398)

**R2.2)** *The risk standardized mortality rate is a standard measure, but the risk adjustment to comfort care rates was developed for this analysis. The description of how the risk-adjustment for the comfort care rates was performed was unclear. Presumably, the risk adjustment for mortality accounts for severity of patient illness using the clinical variables listed.  Was the same adjustment applied to comfort care?  Why was this necessary?*

To create risk-standardized comfort care rates, we used the same model as that for RSMRs, except our outcome was comfort care. We clarify that in the Methods. We risk-adjusted comfort care rates to account for variation in case mix among hospitals.

**R2.3)**  *Page 8, line 42. The choice to highlight the slight decrease in mortality rates after adjusting for comfort care for the subset of hospitals at or above the median rate of early comfort care initiation makes it seem like the authors carved up the data to find a significant result.   Please provide a justification for looking at this subset and whether this analysis was planned a priori.*

This analysis was planned a priori. We have modified our interpretation of our results, and have revised the abstract and discussion to emphasize that our main finding was that of no correlation between RSMRs and risk-adjusted comfort care rates. Please also see our response to R1.2 and R1.11.

**R2.4)** *Table 1:  Line 34, proportion of patients with heart failure in hospitals in each quintile.  Why was this <100%, if the registry only included heart failure patients?  Does this mean that, for example in Quintile 1, 70% of patients had a history of heart failure at the time of admission, so for the remaining 30% of patients it was their index admission?  Or did other cardiac conditions qualify patients to be included in the GWTG-HF registry?*

 The reviewer’s first hypothesis is correct. In quintile 1, approximately 30% of patients in the GWTG-HF registry in quintile 1 were admitted for their first heart failure admission. We now change the label of that row to read “Heart Failure prior to index admission”

**R2.5)**      *Page 3 line 36. The term “withdraw care” is inappropriate and perpetuates stigma about abandonment at the end of life.  Please revise to “provide comfort-focused care.”*

 We appreciate this suggestion, agree with the reviewer, and made this change.

**R2.6)**      *Page 7 line 45 “Patients at highest quintiles… tended to be sicker”- the data does not seem to justify this description, and the p-values provided are not for the comparison of lowest to highest but of differences across all categories.  To better describe the burden of disease, use a comorbidity index or multimorbidity measure.  Or just say, patients at hospitals in lowest quintile had lower rates of dialysis than highest rate, without the "sicker" part.*

We agree that a more focused description of results is appropriate, and made the change in wording as suggested.

**R2.7)**      *Page 9 line 32. “it is surprising that some hospitals initiated comfort care on none or very few of their patients.” – given the limitation of the definition of “early comfort care” as described above, this statement is misleading and reflects the analysis but not necessarily what actually happened.  Hospitals included in the study could have initiated comfort care on day 2 and would not have gotten credit. Revise to specify early comfort care, and justify why that is the only relevant timing (if you can).*

 We have modified the Discussion to be more nuanced. We now state:

While the appropriate rate of early comfort care for patients hospitalized with HF is unknown, given that average hospital RSMR is approximately 12% for fee-for-service Medicare patients hospitalized with HF, it is surprising that some hospitals initiated early comfort care on none or very few of their HF patients. It is quite possible that many of these hospitals initiated comfort care for some of their patients after 48 hours of hospitalization. We were unable to estimate the average period of time patients received comfort care prior to dying, the degree to which this varies across hospitals, and whether the length of time between comfort care initiation and death is related to patient and family satisfaction with end-of-life care. Future research on these topics would add to the literature.

**R2.8)**      *Page 9 line 34.  “we did not estimate how often lack of initiation of early comfort care was poorly aligned with prognosis”  - this sentence does not make sense, please revise.*

 We changed this sentence so that it is clearer. It now reads:

In this study, we also were unable to estimate how often early comfort care was not initiated because patients had a good prognosis.

**R2.9)**      *Page 11 line 19. “DNR can encompass a wide range of preferences” – DNR should only apply to resuscitation preferences, though having a DNR code status can be associated with variable overall care preferences.*

We agree. We clarify our wording and now state:

In addition, while studies have found that DNR rates within the first 24 hours of admission are relatively high (median 15.8% for pneumonia; 13.3% for stroke), comfort care is distinct from DNR.

**Reviewer #3**

*The aim of this manuscript was to describe the early comfort for patients with heart failure, and whether hospitals that more commonly initiate comfort care have a higher 30-day mortality rates.  Data was extracted from the American Heart Associations Get With the Guidelines – heart failure registry.  Hospitals were categorized into Quintiles regarding rates of comfort care provided.  Overall, this manuscript is informative, yet was very difficult to teased out the key findings.  I feel that part of the issue may be due to the fact the hospitals were categorized in quartiles.  It may be a lot easier to interpret the tables and results in for example the hospitals were trichomtomized into comfort care rates (low, medium, high).*

Abstract

**R3.1)** *Line 25: Consider defining ‘early comfort care’, provided within 24 hours of admissions*

We clarified the definition in the abstract, changing from on day 0 or 1 of hospitalization to within the first 48 hours of hospitalization.

**R3.2)** *Abstract line 47: please describe the implications of these findings.*

We added the following text describing the implications of these findings:

It will be important to monitor comfort care rates over time, so that hospitals that align end-of-life care with their patients’ wishes are not penalized in efforts to lower mortality rates.

**R3.3)** *Introduction: Line 29: please provide a citation*

We modified our sentence (see below) and added a reference (Wachterman MW et al. Quality of End-of-Life Care Provided to Patients With Different Serious Illnesses. JAMA Intern Med. 2016 Aug 1;176(8):1095-102.). The revised sentence reads:

As a consequence, high-quality care for patients at the end of life is associated with withdrawing life-sustaining or life-extending therapies.

**R3.4)** *Tables:  The tables are very dense with information, is it at all possible to simplify the tables remove variables that are not pertinent to what is discussed in the text.  Reducing the number of hospital categories would defiantly aid in the interpretation of the tables.*

 Table 1 seems to have the most information packed in a small space, especially under medical history. We removed several rows from medical history (COPD or asthma, CRT-P, CRT-D, ICD only, pacemaker) and placed them into an Appendix Table. We also placed Vitals at Admission into the Appendix. This considerably simplifies Table 1.

We left the hospital categories intact, as we thought it important to show the variation across quintiles, but if the Editor thinks that the tables are still cluttered, we could condense in quintile 1, quintiles 2-4, and quintile 5.

**R3.5)** *Within each quintile heading, there are two Ns.  Does one refer to the number of hospitals, and the other the number of patients?  If so, consider making the a little clearer.*

 The reviewer is correct. We add a footnote to the tables stating that N is number of hospitals and n is number of patients.

**R3.6)** *Figures: Consider deleting Figure 1: I am not sure how informative it is.*

 We agree that the original Figure 1 could be improved. We stratified Figure 1 by types of comfort care, as suggested by the Editor, and believes this improves the display. However, if the Editor so desires, we can delete Figure 1.

**R3.7)** *Figure 2: I had a trouble trying to work out how the figure relates to the text.  Please make that a little easier to interpret.*

 We revised our text and now provide the number of sites (54) that constitute the first bar in Figure 2. The bin width for the first bar is 0 to 0.5%.

**R3.8)** *Line 31 – 33 Figure 3:  I feel that a lot more care needs to be taken in describing the content of the figures …and the tables.  This figure shows an extremely weak correlation and the sentence does not aid in understanding this finding.*

 We apologize for the confusing text. We edited our description of the tables (please see response to R2.4 and R3.9), and simplified the tables (please see response to R3.4). We also provide a clearer explanation for Figure 3. We now state:

Hospitals’ 30-day RSMR and risk-adjusted comfort care rates showed a very weak, but statistically insignificant positive correlation (Spearman’s rank correlation ρ=0.13, p-value=0.0660) (**Figure 3**).

**R3.9)** *Page 8, lines 1 – 3: Rephrase this sentence.  It is difficult to talk about something being ‘less likely’ when the finding is not statistically significant*.

 We changed this and now state:

Compared to hospitals in the lowest comfort care quintile, hospitals in the highest comfort care quintile as likely to be academic teaching hospitals (39.9% vs. 47.2%, p-value 0.14) (**Table 1B)**

**R3.10)** *line 47:  Delete the phrase “data not displayed”*.

 We deleted this.

**R3.11)** *Appendix figures:  consider excluding.  They could easily be explained in text*.

 We left the figures in the Appendix. We agree that they could be explained in the text, and we do describe them in the main text. However, for readers who want additional detail, we believe the figures are helpful. If the Editor so desires, we are happy to remove the figures from the Appendix.

**R3.12)** *I would be interested to see what the timeframe across all hospitals in terms of the provision of comfort care.  Then a justification as to why you choose provision of comfort care within 24 hours.  There may be many reasons as to why comfort care is not provided in the first 24 hours*.

We appreciate this suggestion. We created histograms of the distribution of each of the comfort care categories. Due to limits on the number of figures and because the focus of the paper is on early comfort care, we describe the distribution of late comfort care in the main text but put this figure in the Appendix. However, we are happy to move this figure to the main text if the Editor so desires.

We apologize that we did not clearly explain why we chose early comfort care as one of our primary outcomes. We now explain our motivation in the Methods section. Please see our response to E1 for additional details.

**R3.13)** *Line 47: ‘by being the first’… this is a strong statement. please soften it*.

 We eliminate the phrase “by being the first.”

**R3.14)** *In general it would be great to see more reflection of the implications and future direction of this manuscript*.

 We add the following to the Discussion, specifying areas for future research:

We were unable to estimate the average period of time patients received comfort care prior to dying, the degree to which this varies across hospitals or why it might vary, and whether the length of time between comfort care initiation and death is related to satisfaction with end-of-life care. Future research on these topics would help inform providers seeking to deliver better end-of-life care.

 . . . we did not have any information about patient or family wishes regarding end-of-life care, or the exact timing of early comfort care (e.g., day 0 or day 1). The initiation of comfort care usually follows conversations about end-of-life care involving a patient, his or her family, and the medical team. Thus, we do not know if low early comfort care rates represent the lack of such a conversation (and thus poor quality care) or the desire by most patients not to initiate early comfort care (and thus high quality care). This would be an important area for future research.