Reviewer's report

Title: Prehospital transportation to therapeutic hypothermia centers and survival from out-of-hospital cardiac arrest

Version: 2 Date: 1 December 2014

Reviewer: David Seder

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Comments on BMC
1. Is the question posed by the authors well defined?
   Yes
2. Are the methods appropriate and well described?
   Yes
3. Are the data sound?
   Yes
4. Do the figures appear to be genuine, i.e. without evidence of manipulation?
   Yes
5. Does the manuscript adhere to the relevant standards for reporting and data deposition?
   Yes
6. Are the discussion and conclusions well balanced and adequately supported by the data?
   Yes - see below
7. Are limitations of the work clearly stated?
   Yes - see below
8. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
   Yes, though referencing the manuscripts that describe associations between hospital size, teaching status, location, volume, and outcomes after cardiac arrest should be cited. Look for Brandon Carr's work.
9. Do the title and abstract accurately convey what has been found?
   Yes
10. Is the writing acceptable?
    Yes.

Congratulations on an interesting analysis of cardiac arrest admissions to hospitals utilizing therapeutic hypothermia (TH), contrasted with those not
utilizing TH. These are retrospective and hypothesis-generating data suggesting that being admitted after resuscitation from cardiac arrest to a hospital that performs temperature management is associated with improved functional status at 30 days, but not with improved functional status at the time of hospital discharge.

These data are provocative, and a sophisticated statistical approach has been employed in an attempt to correct for bias that is incurred by conscious or unconscious EMS preferences in hospital selection. They agree with prior publications suggesting that admission to larger, urban, teaching hospitals results in improved survival after cardiac arrest, as does admission to a hospital of higher volume.

Strengths of the manuscript include a large sample size, the geographical approach which adds an epidemiological dimension to the work, and the statistical expertise demonstrated by the research team. The manuscript is concise and well written, staying focused on the research question and citing conclusions that are appropriate to the nature of the work.

I have some concerns:

1. Although there is precedent for it, the combined endpoint of death/hospice/SNF placement vs. home/rehab/transfer/other as a surrogate for neurologically "intact" survival is problematic. Rehab vs. SNF placement is often driven by economic or geographical considerations rather than functional status, and the misclassification of a modest number of patients as "good" or "poor" neurological outcome could result in significant changes to the study results. This weakness should be acknowledged, and cited in the study limitations. Although the inclusion of insurance status in the model may correct for this on some level, that correction is incomplete. This should be acknowledged as a minor essential revision.

2. The rates of survival with good and poor outcomes after discharge alive from the hospital seem very uncharacteristic to me - corroborating my concern described above. In the TTM trial and others, hospital survivors typically are described as 70-85% CPC 1-2 at 6 months post-discharge. This makes me worry that your discharge destination scheme has misclassified patients. This should be addressed in the Discussion as a minor essential revision.

3. Inability to include "down time" (from arrest to ROSC) in the model is a weakness that should be recognized. Down time is strongly associated with the severity of brain injury and overall survival after CA, and would help to determine if the severity of illness is truly comparable between the groups, and help correct other biases in the regression model. This is a discretionary revision.

4. The inclusion of PCI in your model - one of the factors in post-resuscitation care that is most consistently associated with improved outcomes, would make the study stronger. This should be considered and if not included, described as a methodological weakness - a minor essential revision.

5. If after your internal discussion you agree that the combined endpoint variable is problematic, it would be reasonable to simply look at survival at 30 days. The
argument for this is that most survivors are in good neurological condition, and you don't have to worry about unmeasured economic, social, and geographical influences on the endpoint - discretionary revision.

6. Finally, I would suggest you replace at least some of the references to therapeutic hypothermia with targeted temperature management. Even if you were evaluating centers that utilize TH, the current discussion is (appropriately) framed as one of TTM, since the best target temperature is very much in question.

David B Seder MD, FCCM

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests