Reviewer's report

Title: Copeptin Measurement as a Marker of Short-, Mid-, and Long-Term Mortality in All-Comers

Version: Date: 4 February 2014

Reviewer: Roland M Bingisser

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This is an interesting and well-written paper on risk-stratification of emergency patients.

Major compulsory revisions:
1) As the data on BNP is available (Heart 2003), it would add to the quality to show if copeptin adds to the risk-stratification achieved by BNP. Suggestion: ROC-curves containing curve overlap copeptin/BNP
2) Multivariate analyses should be presented in more detail, showing that copeptin is an additional, independent predictor of mortality. Readers could more easily understand the message if a baseline model of age, sex, and comorbidity would be used for risk-stratification - and the additional value of copeptin should be shown in such a model.
3) The concept of all-comers may be somewhat overstretched, as only hospitalized patients were enrolled (on average one third of all emergency patients), only patients over 40, and among those 3644 patients in the original cohort, 1320 copeptin levels were analyzed. Please comment and make changes accordingly. Please mention in limitations.

Minor essential revisions:
1) title
as the topic is risk-stratification, why not use it in the title, such as risk-stratification in emergency patients by copeptin?
2) abstract
please give adjusted hazard ratios
"district hospital" is not an international term. inner-city hospital? regional center?
triage is misused in this context (explained below), it should be "disposition", if taking the example of emergency medicine.

3) materials & methods:
page 5, top: of 2506 patients admitted... this does not correspond to the original article this study refers to (3644 patients admitted in this period)

4) results:
...from 1320 patients (58%)... percentage should be referred to the original population of 3644. That excluded patients were randomly spread is believable, but should be shown (comparison of age, sex, co-morbidity, mortality).

Also, a distribution of main diagnoses should be shown.

... reason for missing information was immigration (?) - EMIGRATION? ...at highest modest... please use weak correlation.

... value of copeptin in relation to elevated values of copeptin... did not understand, please explain.

Multivariate model should be explained in more detail: has a standardized co-morbidity index, such as Charlson been used as covariate, or only the 7 clinical variables, of which 4 are related to the heart?

5) discussion:

... please put "unselected" into perspective (see top)

"previous studies": please omit biology from discussion.

Strengths & limitations:

"unselected nature", a weak expression may be preferable.

If diagnostic groups are available, mortality on their background should be discussed. If not available, please state accordingly.

One major limitation should be mentioned: single center study. Population typical for Denmark? Europe? City - outskirts?

Clinical implications:

Copeptin could indeed be used in the ED, but triage, as internationally defined, is concerned with "who should not wait", and is therefore an instant clinical tool. Suggestion: as emergency medicine is concerned with triage, work-up, and disposition (observation, admission to ward or ICU, discharge), the clinical implication could focus on the latter. To give an example could help the reader to understand the concept (what if you knew, your patient has a 7-day mortality of 10.6%, would you discharge him?)

Quality of written English: Acceptable

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

Declaration of competing interests:

Possible competing interest:

As an emergency physician, I feel that the topic of biomarker assisted disposition is emerging and important. Therefore, I could have the tendency to be less critical than in other fields.