Reviewer's report

Title: The role of urine neutrophil gelatinase-associated lipocalin (NGAL) in patients with ST-elevation myocardial infarction

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Reviewer: Josef Dankiewicz

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The role of urine neutrophil gelatinase-associated lipocalin (NGAL) in patients with ST-elevation myocardial infarction
Simona Kirbis, Maksimiljan Gorenjak and Andreja Sinkovic
BMC Cardiovascular Disorders (Submitted: 2015-02-23)

Thank you for the opportunity to read and review this manuscript. Kirbis et al have performed a study on NGAL levels in urine in patients with ST-elevation myocardial infarction. They collected samples upon admission and after 12h. Their aim was to correlate the urine levels of NGAL to markers (biochemical markers, clinical assessment and echocardiography) of heart failure.

In general the manuscript is well written. The research question is well defined although it is not clear if it is clinically relevant. The tables, figures and conclusion require modification. Statistical methods require some changes but the data appears to be sound. For this manuscript to be a sound addition to scientific knowledge the authors need to further explore potential confounding due to kidney damage, not just in a general term but with data from the patient population. They should also consider multi-variate analysis.

• Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

1. Although not necessary to assess correlation I would suggest that the authors consider some type of multivariate analysis to predict acute heart failure. At a minimum this would require a logistic regression model with comorbidities, age and troponin levels. Does including NGAL improve the model?

2. I would recommend reducing the number of variables in all tables. Is it necessary to show data on leukocytes and CRP and three different time points while there is only data on NGAL at admission and 12h? Additionally I recommend that they align the text to the left.

3. The authors should consider what their main question is. Is it the correlation between NGAL and inflammation, or NGAL and development of acute heart failure.

• Minor Essential Revisions (such as missing labels on figures, or the wrong use
of a term, which the author can be trusted to correct)

1. In my opinion the results section is too cluttered with numbers. I recommend reducing the number of results displayed in this section, especially when they are available in a table.

2. I would suggest changing the term correlation to association when discussing a statistical significant chi2-test.

3. The authors should make the main results in table three clearer by moving them to the top of the table. In my opinion EF, Killip >=II, and NT-proBNP are the most interesting results.

Minor comments:
Row 101 - chest rentgenograph. Correct the spelling. The term chest X-ray would also be adequate.

Row 207 – “We know, that” is superfluous.

• Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

1. In reading work on biomarkers it can be quite difficult to appreciate the distribution of the (urine) levels through numbers alone. The authors should include a boxplot or scatterplot of the urine levels of NGAL. This would ideally be dichotomized by acute heart failure. Further, regarding the distribution of NGAL I think it necessary to formally test for normality with a statistical test. If the assumption does not hold differences in continuous variables should with a non-parametric test (the authors already use a non-parametric test for correlation: spearman Rho). The distribution should be shown with IQR.

2. The authors state that NGAL levels correlated (were associated) with acute HF. Although they only state association the obvious clinical use of a biomarker in this case would be to predict acute HF. So even if they don’t state correlation I would like them to comment on the possible confounding due to acute kidney injury (which has been the main use of NGAL in prior studies). It seems to me that large infarctions, longer PCI-times and more lesions are associated both with acute HF and acute kidney injury due to cardiogenic shock. The authors should comment on this and provide data on the incidence of cardiogenic shock and mortality.

3. I would like the authors to comment on how they arrived at the cut-off value of 50ng/ml. Do they have a reference for this? It not they should clearly state how they arrived at that level.

4. The authors provide information on some co-morbidities but prior heart failure and ejection fraction, which is probably the most important factor in this case are not included. If pre-STEMI ejection fraction or NYHA-class is not available I would suggest a binary variable, CHF before STEMI or not.

5. The authors state that mean creatinine was normal. I would be interested in the incidence acute kidney failure and/or the use of renal replacement therapy (if
any).

6. The authors should comment on what normal values of NGAL are in healthy individuals. Does a urine level of 50ng/ml constitute a meaningful elevation. What is the margin of error in the assay?

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests