Reviewer's report

Title: B-Type Natriuretic Peptide versus Amino Terminal Pro-B Type Natriuretic Peptide: Choosing the optimal heart failure marker in patients with impaired kidney function.

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Reviewer: Amiram Nir

Reviewer's report:

Jafri et al. report BNP and NT-proBNP levels in 190 adults with chronic kidney disease, with and without heart failure. They show higher levels of the peptides in patients with renal failure and in patients with heart failure. They divide peptide levels according to CKD severity and show somewhat better ROC curve function for NT-proBNP in the higher CKD severity.

The study addresses an important issue: the effect of renal dysfunction on BNP and NT-pro-BNP levels, and whether the utility of these biomarkers is preserved in patients with renal dysfunction. The subject has been studied in the past, in greater number of patients, however the division to the different CKD severity, was not fully addressed.

This is a well conducted study. There are, however a number of comments:

Major Compulsory Revisions:

1. It is unclear from the methods how many patients had echocardiography done. The authors should provide this figure.

Minor Essential Revisions

2. Regarding the peptide values, Luchner et al. (2005, reference 20), studied stable patients post MI. They report different cut-off values for LVD:
   BNP (Biosite): 75 pg/mL without and 125 pg/mL with renal dysfunction
   NT-proBNP (Roche diagnostic) 100 pg/mL without, and 350 pg/mL with renal dysfunction.

   In the present study for all CKD grades, cut-off values were: BNP (Axym analyzer, Abbott diagnostic) 217-300 pg/mL and NT-proBNP (Roche diagnostic) 800-4500 pg/mL. As NT-proBNP was measured with the same assay, the difference between the two cut off values should be explained.

3. The statistical work was appropriately performed on Log transformed peptide levels however, the true peptide levels (in pg/mL) should be stated in the text and the graphs, as most readers are using the real values.

4. Fig 1:
y axis: Log BNP/Log NT-proBNP should be < 1, please check.
No linear NT-proBNP noted on the graph legend.

5. Remark regarding the lack of correlation between the peptide levels and with LV EF should be made.

6. Ref 13 has nothing to do with the paper:
Hallock GG, Rice DC. Comparison of TRAM and DIEP flap physiology in a rat model.

Discretionary Revisions:

1. Introduction
The sentence “Once pro-BNP enters the blood, it is proteolytically cleaved into the biologically active 32 amino acid peptide BNP and the inactive 76 amino acid peptide NT-proBNP” does not mention the phenomenon of intracellular cleavage of pro-BNP.

2. In the discussion, the sentence “In this study plasma NT-proBNP appears to be affected more by declining eGFR than plasma BNP, in keeping with the hypothesis that its clearance is predominantly renal but the optimal cut point for plasma NT-proBNP in the diagnosis of heart failure is markedly influenced by the severity of kidney dysfunction” could be written clearer.

3. In the sentence: “McCullough et al reported that it would be appropriate to apply diagnostic value of approximately 200 pg/ml in those with eGFR <60 ml/min/1.73m2. Jae Wong Yang et al stated that heart failure could be diagnosed in patients with kidney dysfunction with a cut off 858.5pg/ml with 77% sensitivity and 72% specificity (29).” It is unclear whether referred to BNP or NT-proBNP. Reference 29 is a study on BNP, and it should be clarified in the text.

4. The sentence: “Similar to BNP Study (30) , PRIDE study (19) and also to results reported by Christopher et al (18) higher cut points would be needed for BNP and NT-proBNP to diagnose heart failure for patients with impaired kidney function” could be written more clearly.

5. The sentence: Ideally occult myocardial ischemia which raises BNP and NT-proBNP levels should have been excluded though our study group was free of signs and symptoms of cardiovascular disease” is not accurate as some of the study patients had heart failure.

Level of interest: An article of importance in its field

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