Author's response to reviews

Title: Characteristics Of Acute Congestive Heart Failure with Normal Ejection Fraction and Less Elevated B-type Natriuretic Peptide

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Author's response to reviews: see over
Dear Dr. Melissa Norton:

Thank you very much for your consideration of our manuscript and request for a revised version. We have copy and pasted reviewer’s comments below, and address each one individually. As you will see, we have made every attempt to incorporate these suggestions as thoroughly as possible.

The following is a description of the changes made.

Response to Reviewer

Thank you very much for your kind and constructive comments to our manuscript “Characteristics Of Acute Congestive Heart Failure with Normal Ejection Fraction and Less Elevated B-type Natriuretic Peptide”. In response to your comments, we have made several changes to improve the paper.

1) In light of the current literature, what does the present manuscript offer as new information? Such results obtained from patients with acute HFnEF are contrasting with recent literature, because a large proportion of patients (32%) had BNP levels <100 pg/ml. One can argue that the number of patients with mild to moderate symptoms (NYHA class II) was high (80%) and that patients with radiographic evidence of pulmonary edema was low; this may, at least in part,
explain the unexpected high prevalence of low BNP levels in this patient population. As a second explanation, the percentage of patients with history of open chest surgery (and mitral prosthesis) is high compared to previous studies (see references above). The authors speculate about pericardial disease as the main determinant of signs and symptoms of heart failure in this subset of patients.

Therefore, I am most concerned by the fact that the authors did not discuss their results (which refer to as a specific pattern of HFnIEF) with the more common pattern of HFnIEF (i.e., diastolic heart failure), in which history of mitral valve and pericardial disease are exclusion criteria (ESC recommendations. Paulus WJ et al. Eur Heart J 2007; 28: 2539-). Accordingly, the authors should more clearly emphasize open chest surgery (and mitral prosthesis) as an underrecognized, specific pattern of HFnIEF characterized by low BNP levels, as compared with previous studies (see references by Maisel, Dokainish and Arques cited above); this would make the manuscript much more attractive and scientifically relevant.

Response:
As described in the ESC recommendations, HFnIEF is frequently a difficult differential diagnosis in a work-up for breathlessness in the absence of signs of fluid overload, especially in the emergency room. In these cases, natriuretic peptides are recommended mainly for exclusion of HFnIEF and not for diagnosis of HFnIEF. In patients without BNP > 100 pg/mL and evidence of pulmonary disease, we must consider pericardial disease for the exclusion of HFnIEF. Several echocardiographic parameters have been proposed as ways to differentiate other restrictive HFnIEF from constrictive pericarditis. Nevertheless, the definite diagnosis remains equivocal, and other diagnostic tests or surgical exploration are required.

In response to the reviewer’s comment, we have emphasized history of open heart surgery and mitral prosthesis as an underrecognized, specific pattern of HFnIEF characterized by low BNP levels and discussed this issue in the results (page 8, line 3) and conclusion (page 2, line 19; page 13, line 6) section. We added this information (mitral prosthesis) in the Table 1.

2) BNP levels are influenced by body mass index; such an important variable should be integrated in Table 1 and statistical models.

Response:
Indeed, BMI is important variable for evaluating BNP. We added this information in the Table 1. In the logistic-analysis, BMI is not independent factor for differentiating between B and NB group.
Minor essential revisions:
1) How many patients fulfilled diagnostic criteria for diastolic heart failure proposed by the ESC recommendations (Paulus WJ et al. Eur Heart J 2007; 28: 2539-)?

Response:
Tissue Doppler-derived E/E' has been performed in 25 patients, six of whom belongs to NB groups. According to ESC criteria, we can diagnose 23 patients as diastolic heart failure. One of the rest is NB patient.

2) The term “heart failure with preserved ejection fraction” is not accurate; one would prefer either “heart failure with normal ejection fraction” or “heart failure with preserved systolic function”. The term "B-type natriuretic peptide" is more relevant than "brain natriuretic peptide".

Response:
We have defined systolic dysfunction as EF < 50%. However, this definition is arbitrary, because EF values show unimodal distribution in HF patients (Solomon SD et al. Circulation. 2005; 112: 3738-3744). For this reason, we used the term “preserved EF”. In response to the reviewer’s comment and according to ESC guideline, we have changed the term “preserved ejection fraction” to “normal ejection fraction”.
In response to the reviewer’s comment, we have changed the term “brain natriuretic peptide” to “B-type natriuretic peptide”.

3) Maisel (author) is misspelled in the text and in reference 4.

Response:
We apologize for this misspelling in reference 4. We have corrected this misspelling.

Thank you in advance for your consideration/

Sincerely yours,

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