

3 August 2014

Fang-Fang Ji,
Science Editor
World Journal of Cardiology

Dear Editor,

Thank you for your letter of 27 May 2014. We were pleased that the Reviewers found our manuscript "**Neuroticism Personality Trait is associated with Quality of Life in patients with Chronic Heart Failure**" of interest and thank them for their constructive comments. We have thoroughly revised the manuscript in accordance with their suggestions, and consider it greatly improved as a result. We respond to the Reviewers' and the Editor's comments below in a point-by-point fashion, and have amended the manuscript accordingly. Reviewers' and Associate Editor's comments are in blue type and our responses are in normal type.

We hope that you consider our revised manuscript suitable for publication in the *World Journal of Cardiology* and look forward to hearing from you.

Yours sincerely,

Dr. Lampros Samartzis

Responses to Reviewers' comments:

Thank you for your constructive comments. We have thoroughly revised the manuscript in accordance with your suggestions, and consider it greatly improved as a result. Below, we respond to your comments below in a point-by-point fashion.

Reviewer #1:

This is a very interesting and novel observational study of the effect of

neuroticism on quality of life of a Greek cohort of chronic heart failure patients. The paper reads well overall and reports some novel findings. The authors should however discuss the potential influencing of their results by the gender disparity of their patient population, given that 6 out of their 36 patients were female and female gender alone is known to affect neuropsychiatric traits of patients.

We agree with the reviewer that gender may correlate with neuropsychiatric characteristics. Nevertheless, due to the small number of female patients in our sample, it was not correct from statistically point of view to be performed gender-specific analysis with between-gender comparisons. In order to make this limitation clear for the reader, we add a relative comment in the limitations paragraph of the discussion section of the manuscript.

Reviewer # 2:

Dear Editor and authors, the manuscript reads OK and has a relevant message for patients with heart failure. Overall the quality of the analysis is reasonable as well as the interpretation of the data. AS the authors state: Personality traits have been shown to affect Quality of Life (QoL) in patients with Chronic Heart Failure (CHF). The aim of this study was to evaluate QoL in CHF patients in relation to the personality trait of Neuroticism and CHF severity". I do have a small problem what the study adds to current literature and novelty. In the revised version of the manuscript the authors should convince the readers the manuscript adds something to existing literature.

Major issues:

1. novelty of findings

Taking into account reviewer's constructive comment, we add the following text under the subheading "innovations and breakthroughs" of the "comments" section of the manuscript: Our study provides additional evidence for the hypothesis that personality factors affect QoL in CHF. More specifically, we found that the personality trait of Neuroticism is associated with QoL independently of the CHF severity. To our knowledge this study is the first to show that the personality trait of Neuroticism, estimated by the NEO-FFI, affects QoL, in CHF patients after adjustment for disease severity evaluated by a symptom-limited cardiopulmonary exercise test, a very accurate modality for detailed assessment of exercise capacity.

2. association between QOL and neuroticism - any association between gender differences? - any association between severity of heart failure and outcome - any association between duration of heart failure and outcome?

Due to the small number of female patients in our sample, it was not correct from statistically point of view to perform gender-specific analysis with between-

gender comparisons. In order to make this limitation clear for the reader, we add a relative comment in the limitations paragraph of the discussion section of the manuscript.

The severity of CHF affects QoL independently of personality, according to the equation presented in table 4.

The duration of disease was not used as a descriptive variable in our analysis, as it is not theoretically possible to affect personality traits of the patients. According to published studies (references 34-37), personality is stabilised after puberty, in the early adulthood, and remains almost stable for the rest of the life so it is unlikely that the CHF duration affects personality. However, the duration of heart failure might affect QoL although it is not always easy to extract the accurate CHF duration from the medical history of the patient. Since we have not included the CHF duration in our assessment, we cannot exclude a possible association between CHF duration and QoL. Taking into account this constructive comment of the reviewer, we now also discuss the absence of duration-of-disease analysis in the limitations paragraph of the discussion section of the manuscript.

3. is it possible to look at QOL/neuroticism and the patients' compliance? Maybe this is associated with the outcome of the study.

We agree with the reviewer that there is a possibility that neuroticism could be correlated with patients compliance (or adherence) pharmaceutical and/or non-pharmaceutical (eg exercise training rehabilitation) treatment interventions. Nevertheless, in this cross-sectional study there were no available data on patients' compliance. It could be interesting to follow-up patients in another prospective cohort study, in order to explore if CHF patients Neuroticism score show any (positive or negative) correlation with compliance/adherence to treatment.

Minor issues: - explain the rationale why ventilation parameters are the main riskmarkers studied in this regard. Do you mean the same with VO₂ peak as Vo₂max measurements as considered standard in HF literature? - it is not directly clear from the methods section which variables were included in the multivariate analysis and why. Does it include age? LVEF? or only the questionnaire and two ventilatory parameters?

In order to assess prognosis in CHF, CPET can provide strong risk markers that have been shown to predict independently mortality in CHF. The traditional gold standard measurement that reliably and accurately measure exercise capacity is the VO₂ peak (the average of the VO₂ during the last 20 sec of a symptom-limited CPET) which has been included in our analysis. VO₂ max (the highest value of VO₂ during symptom-limited CPET) is not commonly used in clinical practice since it cannot be achieved by CHF patients.

We have also used ventilation variables for assessing severity of CHF and in particular VE/VCO₂ slope. This parameter has been extensively shown during the last decade to be a strong independent predictor of mortality in CHF patients and might be a more accurate prognostic index than VO₂ peak in CHF. For these

reasons we have considered both VE/VCO₂ slope and VO₂ peak in risk stratification of our population. Age and LVEF have not been used in the multivariate model.

Reviewer # 3:

The authors present here a nice paper on Heart failure. The objective of this study was to evaluate QoL in CHF patients in relation to the personality trait of Neuroticism and CHF severity. The paper is pretty well written and the results are reasonable. Discussion is correct and the conclusion is supported by data. I think the study is well conducted and it is interesting, since it has a clinical implication. I would only arise a question here, that could be included in the discussion area. This relationship could be influenced by the date of HF diagnosis (i mean, acute long term chronic?).

We thank the reviewer for this comment. All individuals that included in the study were stable CHF outpatients at optimal medical treatment. No acute HF patients were included in the study. The duration of disease was not used as a descriptive variable in our analysis, as it is not theoretically possible to affect personality traits of the patients. According to published studies (references 34-37), personality is stabilised after puberty, in the early adulthood, and remains almost stable for the rest of life. However, Although duration of diagnosis it is not theoretically possible to affect personality traits of the patients, it might affect QoL. Taking into account this constructive comment of the reviewer, we now also discuss the absence of duration-of-disease analysis in the limitations paragraph of the discussion section of the manuscript.

References

34. Costa PT, Jr., McCrae RR. Personality in adulthood: a six-year longitudinal study of self-reports and spouse ratings on the NEO Personality Inventory. *Journal of personality and social psychology*. 1988;54:853-63 [PMID: 3379583 DOI: 10.1037/0022-3514.54.5.853]
35. Terracciano A, Costa PT, Jr., McCrae RR. Personality plasticity after age 30. *Personality and social psychology bulletin*. 2006;32:999-1009 [PMID: 16861305 DOI: 10.1177/0146167206288599]
36. McCrae RR, Costa PT, Jr., Arenberg D. Constancy of adult personality structure in males: longitudinal, cross-sectional and times-of-measurement analyses. *Journal of gerontology*. 1980;35:877-83 [PMID: 6969272 DOI: 10.1093/geronj/35.6.877]
37. Costa PT, Jr., McCrae RR, Zonderman AB, Barbano HE, Lebowitz B, Larson DM. Cross-sectional studies of personality in a national sample: 2. Stability in neuroticism, extraversion, and openness. *Psychology and aging*. 1986;1:144-9 [PMID: 3267391 DOI: 10.1037/0882-7974.1.2.144]

Comments by the Science Editor:

Please write the abstract as this :

An informative, structured abstracts of no less than 246 words should accompany each paper. Abstracts for original contributions should be structured

into the following sections. AIM (no more than 20 words): Only the purpose should be included. Please write the aim in the form: "To investigate/study/...; MATERIALS AND METHODS (no less than 80 words); RESULTS (no less than 120 words): You should present P values where appropriate and must provide relevant data to illustrate how they were obtained, e.g. 6.92 ± 3.86 vs 3.61 ± 1.67 , $P < 0.001$; CONCLUSION (no more than 26 words).

We changed the abstract accordingly.

Please write a summary of less than 100 words to outline the most innovative and important arguments and core contents in your paper to attract readers.

The requested summary has been added in the manuscript.

Please put the reference numbers in square brackets in superscript.
Please check across the text.

Done.

Please write the comments. Writing requirements

(1) Background

To summarize concisely and accurately the relevant background to the article to enable the readers to gain some basic knowledge about the article and better understand its significance.

(2) Research frontiers

To introduce briefly the hotspots or important areas in the research field related to the article.

(3) Innovations and breakthroughs

To summarize and emphasize the differences, particularly the advances, achievements, innovations and breakthroughs, from other related or similar studies, to allow the readers to assimilate the major points of the article.

(4) Applications

To summarize the practical applications of the research.

(5) Terminology

To describe concisely and accurately any terms that may not be familiar to the majority of the readers, but are essential for understanding the article.

(6) Peer review

To provide the comments from peer reviewers that most represent the characteristics, values and significance of the article, and allow the readers to have an objective point of view toward the article.

The requested comments 1-6 are now included in the manuscript.

Please add PubMed citation numbers and DOI citation to the reference list and list all authors.

PMID (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed>)

DOI (<http://www.crossref.org/SimpleTextQuery/>)

Such as: 1 Nayak S, Rath S, Kar BR. Mucous membrane graft for cicatricial ectropion in lamellar ichthyosis: an approach revisited. *Ophthal Plast Reconstr Surg* 2011; e155-e156 [PMID: 21346670 DOI: 10.1097/IOP.0b013e3182082f4e]

The requested information has been added in the manuscript.