Reviewer’s report

Title: Type D personality is a predictor of prolonged acute brain dysfunction (delirium/coma) after cardiovascular surgery

Version: 3 Date: 22 Feb 2019

Reviewer: Johan Denollet

Reviewer's report:

The authors have been very responsive to the reviewers' comments, and the paper has been much improved. However, there still is some room for further improvement, as indicated by my comments and suggestions.

Abstract, paragraph on Results.

On p. 2, last line, the authors state that: "Based on multivariate analysis, Type D personality significantly increase DCDs …". I think it is important to make clear to the reader which variables were included in the multivariate model. Perhaps, the authors could change this sentence as follows:

"Multivariate analysis showed that Type D personality was significantly associated with increased DCDs (OR:2.8, 95%CI:1.3–6.1), after adjustment for depressive symptoms and clinical variables."

Also, I would suggest the authors to slightly rephrase the last 4 lines in the results section of the Abstract as follows:

"Additionally, there was a significant Type D x depression interaction effect (OR:1.7, 95% CI:1.2–2.2), and depressive symptoms were associated with DCDs in Type D patients, but not in non-Type D patients. Mediation modeling showed that depressive symptoms partially mediated the association of Type D personality with DCDs (Aroian test =0.04)."

Text, Results, Regression model, page 14 (lines 2-7).

The authors state that Type D personality, depression, mSOFA, benzodiazepine and propofol were associated with significantly decreased DCDs (Table 2). However, all of these factors were associated with INCREASED (not decreased) DCDs. Please correct.
Also, they mention in the next sentence that: "Increase in DCDs would have indicated that the factors alone would worsen conscious states in the 7-day post-operative period." This line doesn't run, please rephrase as follows:

"This indicates that these factors were independently associated with prolonged acute brain dysfunction in the 7-day post-operative period."

Results, Table 2, p. 15

In the title of Table 2, the word 'free' needs to be removed:

"Regression model for prolonged delirium/coma [free] days".

In Table 2, the authors report that the 95% CI for Type D personality in model 2 was (1.5-1.0). However, the upper CI cannot be 1.0, and should at least be >2.4. Please correct.

Results, Interaction, p. 17

I would suggest to change the heading "Interaction" (p. 17, first line) by the heading "Moderator model".

The significant Type D X depression interaction effect indicates that Type D personality, as a stable disposition, moderated the association of depressive symptoms with prolonged brain dysfunction. This is also clearly presented in Figure 3: depressive symptoms were only associated with prolonged brain dysfunction in Type D patients, but depressive symptoms were not associated with brain dysfunction in non-Type D patients.

The authors now state that: "The presence of depressive symptoms therefore had a significant effect on DCDs between Type D personality patients versus non-Type D personality (Figure 3). Depressive symptoms can therefore be said to have an additive deleterious effect on DCFDs when combined with Type D personality" (page 17, lines 5-8).

I would like to suggest to modify this statement as follows:

"This interaction effect indicates that Type D personality moderated the association of depressive symptoms with DCFDs; i.e., depressive symptoms had a deleterious effect in terms of prolonged brain dysfunction among Type D patients, but depressive symptoms were not associated with DCFDs in non-Type D patients (Figure 3)."
Figure 3.

The title of Figure 3 (Depressive symptom's interaction for delirium/coma days) is not very informative. Consider changing the title to:

"Association of depressive symptoms with prolonged brain dysfunction, stratified by Type D personality".

The labels on the left side of this figure are a bit misleading. Now it looks like the first two graphs in the forest plot represent the effects of Type D personality. However, what they actually do represent is the effect of depressive symptoms, stratified by Type D personality.

Hence, the following labels would be more informative:

"Depressive symptoms in Type D patients"

"Depressive symptoms in non-Type D patients"

"Depressive symptoms in the total sample"

Figure 4 legends, p. 19 (lines 1-2).

What the figure 4 shows is the mediation effect of depressive symptoms, but not the mediation effect of Type D personality. Hence, the legend of Figure 4 could be something like:

"The mediation effect of depressive symptoms regarding the association of Type D personality with DCDs, adjusted for the same covariates used in regression modeling."

Discussion.

Please discuss the finding that depressive symptoms were associated with prolonged brain dysfunction among Type D patients, but not among non-Type D patients.

Discussion, page 21 (lines 11-13).

The author state that: "… has reported that Type D personality is associated with decreased endothelial progenitor cells in a large, population-based study [52] and a recent study showed that this association was robust across time[53]." However, reference [52] reports findings of a study in patients with heart failure (and not a large, population-based study), and reference [53]
reports on the association of Type D personality with endothelial dysfunction (and not endothelial progenitor cells) in patients with coronary artery disease. Hence, this statement should be corrected along these lines:

"… has reported that Type D personality is associated with decreased endothelial progenitor cells in patients with heart failure [52] and a recent study in patients with coronary artery disease showed that the association of Type D personality with endothelial dysfunction was robust across time[53]."

References
I still noticed some inaccuracies in the reference list.
Ref. #16. The correct authorship of this paper is: Denollet J, Sys SU, Stroobant N, Rombouts H, Gillebert TC, Brutsaert DL.
Ref. #33 does not include the Journal name.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
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