Peer Review File

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Reviewer #1

We thank Reviewer #1 for his valuable contributions. We were eager to implement all revisions as far as possible.

Comment 1: *Intro: „An estimated 1 out of 5000 individuals is affected by MFS": A more accurate number 2 to 17 in 100.000, 0,002 to 0,017% of population, as assessed based on measurements in (1)*

Reply 1: Revision accepted and changed accordingly.

Comment 2*:* *Manuscript throughout: Please restate* "*MFS patients" as* "*individuals with MFS" or similar.*

Reply 2: Revision accepted and changed accordingly to "individuals/patients with MFS".

Comment 3: *Methods:* "*which constitutes the largest ever attempt". Should it be* "*which constitutes the largest attempt ever". Plus: reconsider usage of such superlative?*

Reply 3: Thank you for this comment. The phrase was adjusted accordingly ("which constitutes the first large-scale attempt to comprehensively assess the health care situation of CHD patients in a large ACHD cohort in Germany").

Comment 4: *Methods, population: How did you select your controls? Some info is needed. Propensity score matching? Consecutively? Time interval of recruitment?*

Reply 4: Patients were consecutively included in the order in which they presented at the institution and were not selected in prior. The collectives were not matched for comparison. Recruitment took place between 05/2017 – 07/20. The manuscript was adjusted accordingly.

Comment 5: *Methods, population: were there individuals invited who rejected participation?*

Reply 5: Good note. Tracking a response rate was not possible because the questionnaire was/could be submitted online after the hospital visit.

Comment 6: *Results:* "*Out of 3.885 patients": Out of 3.885 ACHD patients? Please, specify.*

Reply 6: The present study represents a subgroup analysis within the ongoing cross-sectional research project VEMAH. It included 3.885 ACHD out of which 102 patients suffered from MFS (compare updated "Method" section) .

Comment 7: *Results: Your comparisons may be more meaningful if you could provide (maybe in the methods) some kind of characteristics of the population beyond "ACHD".*

Reply 7: Unfortunately, we are not able to provide further background characteristics of the population since all data is patient-reported.

1. *von Kodolitsch Y, De Backer J, Schüler H et al. Perspectives on the revised Ghent criteria for the diagnosis of Marfan syndrome. The Application of Clinical Genetics 2015: 8: 137—155.*

Reply: Thank you for this valuable reference. It was included into the manuscript.

Reviewer #2

We are very grateful for the revisions of Reviewer #2. We made considerable effort to implement all revisions. Additionally, the manuscript was edited for grammatical and syntactic errors by a scientific editor.

Comment 1: *Please specify and articulate which phenotypes are examined, it is unclear whether all MFS satisfied the Ghent criteria. That is the same for congenital heart defects (CHD), CHD present a wide spectrum of heterogeneous morphological phenotypes of cardiac anomalies.*

Reply 1: We agree 100%. Within the context of this study, leading diagnosis was **patient-reported**. The veracity of their medical condition therefore remains unclear. This was also included as a major limitation. However, according to empirical findings chronically ill patients are commonly better educated about their medical condition compared to the general public.

Comment 2: *Title, please revise and correct accordingly- there is no need to use abbreviations in this section.*

Reply 2: Thank you, revision accepted. The title was accordingly modified to avoid misconceptions. (Quality of Life in Patients with Marfan Syndrome: A cross-sectional study of 102 adult patients)

Comment 3: *Abstract, please revise and correct. Start directly with a clear message, the authors used clinical data retrospectively of heterogeneous clinical phenotypes, are MFS treated and how?*

Reply 3: Thank you for this input. We adjusted the abstract to specify the study more precisely. As mentioned in Reply 1, all information was based on patient-reported outcomes and medical data may have been classified incorrectly due to a patient's limited knowledge of his or her condition. Subsequently, it would be advisable to synchronize these data with medical records in the future.

Comment 4: *Background, please revise, correct, and cite correctly. "Quality of life" concept as being multidimensional, compromising: Classic domains such as physical, mental, emotional, and social functioning, with fatigue, pain, emotional distress, social activities and roles being important factors…., why is it important to study only the psychological situation of MFS patients????*

Reply 4: Background was updated content wise. Since clinical research traditionally focused on "hard" outcome measures, such as morality, morbidity and functional status, the concept of QOL has become increasingly recognized as an important patient reported outcome measure in the evaluation of care and treatment. Further, increased attention on the psychological situation of MFS patients is especially important as MFS is a multi-organ disease which may lead to severe psychosocial impairments in adult life.

Comment 5: *Methods: At least more than one method must be used to design such studies. Using only the EQ-5D-5L is not satisfied. Please add (table) with adequate patients demographic.*

Reply 5: Patient-reported outcome measures (PROMS) were assessed by a specifically devised questionnaire complemented by the EQ-5D-5L which consists of a descriptive system and the EQ visual analogue scale (https://euroqol.org). Table 1 was adjusted.

Comment 6: *Results, tables are very confusing to read, kindly revise. Figure is unclear, please revise and add legends.*

Additional explanatory information was included (**"**Figure 1 represents 5 dimensions of the EQ-5D-5L. Each dimension consists of 5 levels ranging from no problems, slight problems, moderate problems, to severe problems and extreme problems. Average values were calculated for both dimensions and accordingly depicted"). For a better understanding and readability the manuscript was additionally revised by a scientific editor.

Comment 7: *Discussion and conclusions please revise and follow guidelines.*

Reply 7: We adapted the manuscript to STROBE Guidelines for epidemiological studies. In addition to linguistic revisions the order of sections was changed accordingly. The STROBE checklist is completed and attached.

Comment 8: *References please revise and update.*

Reply 8: References were revised and udated.