Reviewer's report

Title: Prevalence of valvular heart disease in nonagenarians from the general population: The Leiden 85-plus study

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Reviewer: Giovanni Gambassi

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DISCRETIONARY REVISIONS

The title focuses only on the prevalence of valvular disease whereas a more appropriate one would integrate the relation with activities of daily living or with physical function in some way.

The word “competence” to describe the performance of an individual in the activities of daily living is a bit awkward.

The introduction section in my opinion should be focused more on the specific topic rather than give an account of the effect of age on anatomical and functional parameters. It reads more as a textbook rather than a scientific manuscript.

In describing the study protocol, the authors mention that “...performance tests were conducted” when person became 90 years old. To what exactly do they refer to. The GARS is only a questionnaire. Do the authors have available data on functional performance tests (6 min WT)??

MAJOR COMPULSORY REVISIONS

A para on the limitations of the current study seems warranted. In particular, the authors need to mention and justify several problems arising from the study. First, 705 85+ individuals were asked to participate and then later the cohort is suddenly down to 599 individuals. Clarify this aspect. Following, 290 individuals reached 90 years which would translated in 50% of the initial cohort dying. The authors should convince the reader that their study is not affected by an evident survivorship effect. For example, a prevalence of only 48% for cardiovascular comorbidity seems to lend support to such bias. Could equally prevalent and sever valvular heart disease have been associated with reduced physical performance in individuals who died before reaching 90 years? Do baseline characteristics of the dead (at their initial or last? Available assessment) resemble those of the study sample?. Of the 290 individuals reaching 90 years, 81 underwent echocardiography. The authors state that the “...remaining 175 …were not able to visit the study center.” Clearly, 81+175 does not add to 290!!! Also, the authors should provide evidence that those who did not show up and did not receive echocardiography were not different, at least based on the parameters continuously collected. This is of fundamental importance in order to be able to exclude a dramatic selection bias. The authors should also discuss the
limitations of their measure of the outcome. ADL, IADL or the GARS score which combines them might not be the most appropriate measurement and other performance test could prove more sensitive and accurate. Or, it could be just that the performance of the individuals in this cohort was too skewed towards very little impairment (bias??).

A very confusing issue regards the definition of what the authors refer to as either “significant”, “clinically relevant” valvular heart disease. This seems to have different meaning in different section of the manuscript. Also, it does appear to have a variable relation with the severity of the disease based on the ACC/AHA guidelines. As clearly stated in the methods section on page 6, the authors considered that significant (clinically relevant) were

- Mitral stenosis of any severity
- Aortic stenosis of any severity
- Mitral regurgitation of only moderate-to-severe severity
- Aortic stenosis of any severity
- Tricuspid regurgitation of only moderate-to-severe severity

All this requires a clear and convincing explanation. Why didn’t the authors adopt a common definition? Do the results change is they select only those with moderate-to-severe valvular disease individuals? On the same line, authors should refrain from assuming that their data refer to only moderate-to-severe disease (as in discussion, page 12)

MINOR ESSENTIAL REVISIONS

The abstract in its present form reads rather generic since it refers continuously to “significant valvular disease…” for which no definition is given. So, for a general readership the abstract is hard to follow.

The numbers presented in the abstracts are at odds with those presented in the results section. Authors should check them very carefully and possibly provide an explanation for such inconsistencies. A significant valvular disease is reported to occur in 57 (70%) individuals while in the result section this becomes 61 and 75%.

In the introduction section, the authors state that the aim of the study was to “..evaluate ….the prevalence of significant (moderate to severe) left-sided …” This is not true. First, although the authors state throughout the manuscript that they are studying “significant valvular disease” this is not equivalent to moderate to severe. In fact, in the methods section at page 6, it is clearly reported that mitral stenosis and aortic regurgitation were considered significant even if mild according to ACC/AHA guidelines. Secondly, the paper will then constantly consider tricuspid valve as well, thus, including right ventricle.

It is the opinion of the reviewer that much information about the study population should be given in a revised table 1. Since the GARS score combines info on IADL as well, table 1 should include living and social descriptors. Also, information on clinically relevant conditions should also be mentioned.
Performance on activities of daily living is clearly a mono-dimensional estimated of cardiac function. Similarly, if the authors have available information on medications those would be much informative.

GARS scores ranged from 18 to 69, a quite substantial span. Could the data be analyzed according to tertiles of baseline function?

A figure with the prevalence of the most common combination of valvular disease would be helpful.

The discussion should offer a convincing explanation of why the study population suffered such an extremely high prevalence of valvular disease but in contrast to the currently available data, aortic stenosis was only rarely documented. Isn’t this awkward?

One of the authors contributed a paper years ago on ways to discriminate between statistical vs clinically meaningful changes in scales of physical performance. It is the reviewer’s opinion that results of new analyses, especially by valve severity, be interpreted in this light.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

'I declare that I have no competing interests'