Reviewer’s report

Title: QUALITY of life, satisfaction and outcomes after ministernotomy versus full sternotomy isolated Aortic Valve Replacement (QUALITY-AVR): study protocol for a randomised controlled trial

Version: 0 Date: 28 Nov 2017

Reviewer: Michael Madsen

Reviewer's report:

Overall impression:

The current trial protocol investigates a clinically relevant problem in patients undergoing major cardiovascular surgery. The minimally invasive MS strategy is compared to the FS standard approach which even in light of the TAVI procedure is a relevant question. However, the manuscript in the current form lack important information and structure that needs to be provided. The authors could benefit from following the SPIRIT guidelines to the letter.

Title

The current title is too long and repeats itself unnecessarily. The acronym (QUALITY-AVR) should be moved before the :, and it should be mentioned the study is a protocol. A possible title could read:

"QUALITY of life, satisfaction and outcomes after ministernotomy versus full sternotomy isolated Aortic Valve Replacement (QUALITY-AVR): a protocol for a randomized controlled trial."

Abstract

The abstract is overly detailed regarding the sample size calculation which should be addressed in the method section.

The sentence line 15-17: ("J" shaped upper hemisternotomy toward right 4th intercostal space) should be deleted.

Drop the notation Major secondary endpoints. The sentence describing secondary endpoints is cryptic and should be rewritten.
The first sentence in the abstract discussion describes several aims, which should be broken into separate sentences. The wording a "positive" result is unfortunate and should be rephrased.

Major issues

BACKGROUND

* In all a well written background. It is clearly argued that MS is superior to FS in many aspects; however, the reason to choose a patient reported outcome as the primary outcome is not clear. It could be argued that the proper trial to perform would be the trial with mortality as an outcome. As the background reads now, it seems the patient reported approach was chosen in light of the lower sample size and feasibility to perform a trial in a single centre setup.

A patient centered approach is highly relevant, however, this choice needs to be argued in the background.

* Page 4 line 9-16 is one long sentence and needs to be broken into two. Furthermore, it is unclear from the sentence if MS was apart of the PARTNER or PIVOTAL trials. This needs to be clear.

* Again "quality of life, satisfaction and outcomes " are all mixed into one. These needs to be described as separate specific aims.

METHODS

* The structure of the method section should be rearranged so it follows the SPIRIT statement.

* No SPIRIT figure is provided which is essential to follow the SPIRIT statement which is required by the Trials Journal.

* The method section mentions a pragmatic and independent design. How is this and why is it relevant for the current trial? Does the authors mean researcher initiated or ?

* The details regarding ethical approval and registration should be placed in a separate section. Again adhere to the SPIRIT guidelines.

* The authors have a tendency to write to long sentences, which makes the manuscript tedious to read. Throughout the manuscript this needs to be addressed.
* The "EuroQoL 5" was chosen as it was tested in a Spanish population. Is this the same as a validated translation. Please give references in this regard. The current reference is internet reference to a Spanish website, which is irrelevant to the reader.

* No reference is given to the SATISCORE®. Furthermore it is unclear, how the total score is 100 when the text mentions 20 statements with 6 possible outcomes (120 total). More specific information needs to be provided.

* Multiple assessment are performed on multiple outcomes, however, the timing is unclear from the current manuscripts. Produce a spirit figure and reference it actively to help the reader instead of confusing the reader.

* In the "selection of patients" section: "current clinical practice and meet the inclusion and exclusion criteria" drop "the inclusion and" as they are mentioned in the text just before.

* Block randomization is mentioned. Why was this chosen in a single centre study? Do the authors mean stratification on a given variable instead?

* AleatorMetod is mentioned as a computer randomization program. Give a reference or delete if not relevant.

* Allocation concealment is briefly described as performed by an administrative officer. Who are the medical personnel? Is the patient intended to be blinded? If so describe in detail how this is achieved. The study is described as single-blind, however, no follow-up description is given. Is the outcome assessor blinded and who assess the different outcomes ? Provide sufficient detail so the study could be replicated.

* The study endpoint is written in bold text. Why is this ? The description is of two interventions, however, the current trial test MS (active treatment) against FS (control/standard of care) write this instead.

* Several combined endpoints regarding complications are mentioned. Furthermore, the MAC are nested within the other. This constitutes a reporting issue and should be discouraged. Composite outcomes are problematic as the direction of interventions effect could balance each other out. So separate incidences should be reported.

* Nosocomial infections are mentioned, however, the time period is one month postoperatively. Does the authors expect the patients to be hospitalized for an entire month. Are infections at home not a relevant complication?

* Postoperative stay in total and in the intensive care unit are mentioned as outcomes. The correct terminology is length of stay (LOS) and should be changes accordingly. When reporting hospital stay it is vital to report if the unit had ERAS protocols in the department and what were the discharge criteria. This could be provided as supplementary material.
STATISTICAL ANALYSIS and sample size

* As the authors also correctly address the SD of 0.15 and MID of 0.10 are arbitrarily chosen on the best available information resulting in a 2 x 48 setup and planned inclusion of 100 patient. I.e. expected drop-out of 4 patients over 12 month period.

Such a low drop-out rate is overly optimistic and will only likely result in an underpowered trial. Will additional patients be recruited.

* The authors have chosen a repeated measure design (1, 6, and 12 months), however, not specified a repeated measure analysis for the primary outcome. T-test will be used (depending on distribution) to test group differences, however, a mixed model analysis would be a more appropriate analysis model.

* Distribution of data will be tested using the Kolmogorov-Smirnov test. Why not use the histograms or QQ plots to assess distribution. If relevant do the authors intend to use transformation of data?

* No information regarding how "missing data" will be handled is provided. This needs to be described in detail.

* "Effectiveness of treatment" is described in the end of the statistics section, however, no measure is given.

* Description of the intention to treat and per protocol is insufficiently described. This needs to be detailed and related to the planned analysis.

* The statistical section could greatly benefit from a consultation from a statistician and be described in a detailed analysis plan.

SUMMARY AND TRIAL STATUS

* No details regarding data-sharing policy is described in the current protocol. This needs to be described in detail.

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