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

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Reviewer: Jaw Yuan Wang

Reviewer's report:

Reviewer(s)' Comments to Author:

Rodriguez-Caulo et al. report the study protocol of "QUALITY of life, satisfaction and outcomes after ministernotomy versus full sternotomy isolated Aortic Valve Replacement. Rationale and design of the QUALITY-AVR trial". The trial is a single-blind, single center, randomized clinical trial that compares two treatment groups: 100 patients undergoing aortic valve replacement (AVR) with full median sternotomy (FS) or with ministernotomy (MS). The primary end point measure is to detect differences between the two intervention groups greater than or equal to 0.10 points change from the baseline questionnaire EQ-5D-5L® Index, at 1, 6 or 12 months after the surgery. Major secondary end points are the differences in change from other baseline EQ-5D-5L® utilities (Visual Analogue Scale, Health Index and Severity Index), SATISCORE® (cardiac surgery specific satisfaction questionnaire), a combined safety end point of 4 major adverse complications at 1 month (mortality, acute myocardial infarction, stroke or transient ischemic accident and acute renal failure) and 1 year survival. Other secondary end points are differences in bleeding the first 24 hours, intubation time, postoperative hospital stay, intensive care unit stay and transfusional needs the first 72 hrs. Authors anticipate this trial could modify the surgical "Gold-Standard" for aortic stenosis surgery, and subsequently the need to change the control group in transcatheter aortic valve implantation trials.

Major Compulsory Revisions:

1. The study design was a single-blind, single center, randomized clinical trial. I am wondering if it is a real single-blind clinical trial as surgeon and patient would realize the FS vs. MS after surgery and masking of the surgeon and patients would be difficult.

2. Sample size was determined for primary end point with an alpha error of 0.05 and with a power of 90% in detecting differences between intervention groups ≥0.10 points in change from baseline quality of life Questionnaire EuroQOL-index (EQ-5D-5L®), measured at 1, 6 or 12 months. The first concern is which time point would be considered as for the measurement of comparison? Two groups of 48 patients are necessary for a minimum of
n=96 patients. In view of possible losses to follow-up, 100 patients will be randomized. The potential loss of follow-up or drop is less 10%, of which is relatively low than the average loss in clinical trials. In addition, several secondary points were clearer than the primary end point as the determination of sample size and might be better when compared to the primary end point as its clinical importance.

3. Both groups of patients will receive clinical follow-up and complete the EQ-5D-5L® quality of life questionnaire at 1, 6 and 12 months, and SATISCORE® at 1 and 6 months. Why did not add an additional 12-month of SATISCORE® questionnaire assessment?

4. The primary endpoint measure is to detect differences between the two intervention groups greater than or equal to 0.10 points change from the baseline questionnaire EQ-5D-5L® Index, at 1, 6 or 12 months after the surgery. The 0.10 point change is really less different and significant? In addition, authors used the quality of life as the major determination as it would be hard to actually reflect the superiority of MS to FS in clinical practice.

5. Authors anticipate this trial could modify the surgical "Gold-Standard" for aortic stenosis surgery, and subsequently the need to change the control group in transcatheter aortic valve implantation trials. Please describe in more details how this trial would change the control group in transcatheter aortic valve implantation trials as it might be considerably different viewpoints in the study design between two clinical trials.

6. In abstract section: to date, few clinical trials have been conducted that compare AVR surgery using MS versus FS, and no significant differences have been found, due to inadequate design, a lack of statistical power or a sample size too small for the primary endpoint of mortality, although significant differences did exist in morbidity on the side of MS (lower rates of pain, transfusions, bleeding, mechanical ventilation time, stay in intensive care and hospital…etc.). However, the current study design still not yet provide the most important information or elements to readers or even probably lead to misunderstanding regarding the role between FS and MS under the current study design.

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