Author's response to reviews

Title: Determination of mitral valve area with echocardiography, using intra-operative 3-dimensional versus intra- & post-operative pressure half-time technique in mitral valve repair surgery

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Object: MS: 1406268632860444 - Determination of mitral valve area with echocardiography, using intra-operative 3-dimensional versus intra- & post-operative pressure half-time technique in mitral valve repair surgery

Woon-Seok Kang, Jae Won Choi, Joo-Eun Kang, Jin Woo Chung and Seong-Hyop Kim

Thank you for consideration of our manuscript for publication in your journal. We have reviewed above manuscript according to reviewer’s comments.

Reviewer #1 (Dr. Rocío García Orta)

Major compulsory revisions:

1. From 107 patients between April 2011 and March 2012, there were 57 patients without 3d study. Was it because of poor image quality or because the operator didn’t apply this method for some other reason? Which was the criteria applied to select these patients?

- As mentioned in the methods, our inclusion criteria was the patients who had elective mitral valve repair surgery due to mitral valve stenosis (MS) (> moderate degree) or mitral valve insufficiency (MR) (> moderate degree) in our hospital from April 2011 to March 2012.
- In our hospital, there were two operating room for cardiac surgery and two different echocardiographic platform [GE without 3 dimentional (3D) platform (Vivid7 Dimension, GE medical systems, Horten, Norway) and Philips with 3D platform]. Therefore, the excluded 57 patients had been underwent mitral valve repair surgery (MVR) with GE echocardiographic platform.
- There were no patients with the inadequate recorded 3D images for determination of mitral valve area (MVA) by 3D planimetry because the acquisition of 3D images was standardized. (page 6 in the manuscript).
  - The detailed description was contained in answer to question 2.
The reason of exclusion for 57 patients was added as below (page 8 in the manuscript).

“57 for examinations only under 2D TEE platform without availability of 3D TEE, 19 for other concurrent valvular surgeries, 4 for low LV function (LV ejection fraction <40%), and 1 for MR grade >moderate at intra-operative post-MVR period. There were no patients with inadequate the recorded 3D images for determination of MVA by 3D planimetry technique.”

2. Did any of the 26 3d echo studies have non interpretable or bad quality images?

• There were some differences in the quality of restored 3D images for mitral valve (MV) apparatus. However, the acquisition of 3D images was standardized. Therefore, the recorded 3D images were enough to measure the MVA by 3D planimetry technique.
• The detailed description for acquisition of 3D images was added as below (page 6 in the manuscript).
  “3D full-volume images or 3D zoom images for an “en face” MV view from the left atrium (LA) or left ventricle (LV) perspective were acquired. The recorded 3D images were checked whether they contained whole structures of MV including anterior mitral leaflet (AML), posterior mitral leaflet (PML) and mitral valve annulus. If they did not contain the whole structures, the 3D images were re-acquired.”

3. The authors should explain the reasons of the high variability of the 3d method valve area measurement: limited image quality? Differences in the selection of the gain by the different observers?

• We described the reasons for differences of measured MVA between pressure half time (PHT) technique and 3D planimetry technique in discussion session (page 11-12 in the manuscript). The values of MVA derived 3D planimetry technique were obtained from the same recorded 3D image by different 3 observers (cardiac anaesthesiologist at operating room, observer A, observer B). Therefore, the variability of the 3D planimetry technique might be associated with individual differences for measurement process such as detection of the exact posterior mitral leaflet (PML) and tendency of marginal tracing to detect MVA.
• Additionally, measurement of PHT is done by drawing a straight line from vertex along slope whereas measurement of MVA by 3D planimetry technique is done by marginal tracing of AML and PML. Therefore, more complex measurement method than PHT technique may be associated with higher variability of 3D planimetry technique.
• We described the details for variability of 3D planimetry technique as below (page 12, 13 in the manuscript). “The ICC values for the PHT technique and 3D planimetry technique with TTE were 0.90 and 0.78, respectively, and the ICC value for the PHT technique with TTE was 0.91. These values showed acceptable inter-observer variability. However, relatively lower ICC value of the 3D planimetry technique compared with that of the PHT technique means higher variability of 3D planimetry technique than PHT technique. And, this might be associated with above mentioned two reasons, namely the influence of the flexible strip to 3D image and the different observer’s tendency to detect the MVAs. Usually, the measurement of PHT was done by drawing a straight line from vertex along slope whereas the measurement of MVA by 3D planimetry technique was done by marginal tracing of AML and PML. Therefore, more complex measurement method than PHT technique might affect to the higher variability of 3D planimetry technique.”

4. I think it must be stressed that the study doesn’t show that 3d method is inaccurate for the determination of valve area because there is no gold standard to compare it with. Accuracy of THP measurement of mitral valve area has been demonstrated empirically for rheumatic mitral stenosis, but not for non-stenotic valves or for other etiologies as after mitral valve repair, and therefore it shouldn’t be considered the reference method in this setting. In fact, some studies have found that immediately after valve repair, THP underestimates mitral valve area compared to 2d planimetry, which is usually considered the reference method in mitral valve area estimation (2).

• We agreed reviewer’s opinion. The aspect that 3D planimetry technique was not inaccurate for the determination of MVA because there is no gold standard to compare it with was the focus of our article. Therefore, in discussion session, we mentioned this point twice, and we emphasized by separating what we want to say to conclusion session as below (page 14 in the manuscript). “The above reasons might be associated with the difference between MVAs by 3D planimetry technique and PHT technique in the present study. In other words, the reference values for MVA using the 3D planimetry technique would be different from that using the PHT technique after MVR.” “MVA measured by 3D planimetry technique with TEE at intra-operative post-MVR period was larger than that by PHT technique with TTE at post-operative period. However, it did not mean that the 3D planimetry technique was inaccurate but needs cautions at determination of MVA using different techniques.”
As mentioned in introduction session, the measurement of MVA by 2D planimetry technique with TEE after mitral valve repair surgery (MVR) is usually unfavorable and meticulous effort is required because of difficulty to acquire a proper 2D image plane. Therefore, in our institution, 2D planimetry technique for MVA measurement after CPB weaning was not applied. This was the reason that we did not use the value of MVA derived by 2D planimetry technique with TTE as reference value. Instead of using the values of 2D planimetry technique, we used the values derived by PHT technique with TTE at postoperative day 7. In addition to the description in discussion session, the reason for using MVA derived by PHT technique with TTE at postoperative day 7 as reference value was to compare the MVAs measured by same technique.

We described as below in discussion session. (page 11 in the manuscript)

“The other reason for using the MVA derived by PHT technique with TTE at postoperative day 7 as reference value instead of that derived by 2D planimetry technique was to compare the MVAs measured by same technique, because our cardiac anaesthesiologist did not measure the MVA by 2D planimetry technique after CPB weaning due to difficulty to acquire proper 2D image.”

4. I don’t consider pulsed Doppler the most appropriate method in the measurement of THP. The guides in valve stenosis (4) recommend the use of continuous Doppler unless there is something that prevents its use. Pulsed Doppler measurements can be variable depending on the sample volume location.

We strongly agreed reviewer’s opinion. In the present study, only 4 patients of 26 patients were mitral valve stenosis. And, in cases of mitral valve insufficiency, our cardiac anaesthesiologist and cardiologist measured PHT with pulsed wave Doppler, and in cases of mitral valve stenosis, they measured PHT with continuous wave Doppler.

The details of measurement for pressure half time were described as below (page 6 in the manuscript).

“Three consecutive velocity-time integrals (VTI) of mitral inflow Doppler were traced by placing the sample volume of the pulsed-wave Doppler for MR or continuous-wave Doppler for MS on the tip of the MV leaflets in a mid-oesophageal aortic valve long-axis view.”

5. In some studies, PHT was compared to other methods to detect significant mitral stenosis after repair, and for example, transvalvular gradient showed better accuracy than PHT (6). The most frequently reported reason is THP dependence of net atrioventricular compliance. But the present study shows good
correlations between intra and postoperative THP. Do the authors find an explanation to the differences with respect to other studies?

- Several studies reported the inaccuracy of PHT technique for MVA measurement and the reasons when immediately after CPB ended in MVR. And some studies reported that other parameter such as pressure gradient was more useful for immediate postoperative MV evaluation to detect MS. On the other hand, Maslow A et al. reported the importance of optimizing haemodynamics during assessment of MVA, and suggested that the PHT method for MVA evaluation after mitral valve repair surgery is still useful.

- According to our institutional standard protocol, our cardiac anaesthesiologist maintained stable patients’ haemodynamic status (mean arterial blood pressure > 60 mmHg, heart rate < 90 beats per minute, cardiac index > 2.0 l.min\(^{-1}\).m\(^{-2}\)) with inotropics and vasopressors when echocardiographic examination was done after CPB weaning and this haemodynamic status might be similar to the state of everyday life. Therefore, the values of MVA derived by PHT technique showed good correlation and were not different although those values were measured at different times.

- We described as below in methods session and discussion session. (page 5-6, page 10-11 in the manuscript)

> “After MVR, successful cardiopulmonary bypass (CPB) weaning and achieving stable haemodynamic state (mean arterial blood pressure > 60 mmHg, heart rate < 90 beats per minute, cardiac index > 2.0 l.min\(^{-1}\).m\(^{-2}\); approximately one hour after separation from CPB), MVA derived by PHT technique with TEE (MVA-PHT1) was determined.”

> “Several studies reported the inaccuracy of PHT technique for MVA measurement, and the reasons such as geometric change of MV structures and net atrioventricular compliance when immediately after CPB ended in MVR [14-16]. And some studies suggested that other parameter such as pressure gradient was more useful for immediate postoperative MV evaluation to detect MS [17,18]. However, Maslow A et al. reported the importance of optimizing haemodynamics during assessment of MVA, and suggested that the PHT technique for MVA evaluation after MVR was still useful if haemodynamic optimization could be made [19,20]. In the present study, according to our institutional standard protocol, our cardiac anaesthesiologist maintained patients’ haemodynamic status stably within the predetermined range by using inotropics and vasopressors when echocardiographic examination was done after CPB weaning. And this haemodynamic status would be similar to the state of everyday life. Therefore, the values of mitral valve area derived by PHT technique showed good correlation and were not different although those values were measured at different times.”
6. Despite the paucity of studies analyzing the problem of mitral valve area measurement after surgical repair, I think that some of the studies mentioned previously are directly related to the subject of the article and should be included in the references.


• Thank you for reviewer’s recommendation. Previously mentioned references 2-4 were included as reference number 14-16, and 5,6 were included as reference number 17,18, and recommended reference 1 and additional Maslow’s other article were included reference number 19,20.

• The additional references are cited in discussion session. (page 11 in the manuscript)