Author's response to reviews

Title: Severity of Aortic Regurgitation Assessed by Area of Vena Contracta: a Clinical Two-Dimensional and Three-Dimensional Color Doppler Imaging Study

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Version: 3
Date: 20 March 2015

Author's response to reviews:

MS: 7726369401589920

Severity of Aortic Regurgitation Assessed by Area of Vena Contracta: a Clinical Two-Dimensional and Three-Dimensional Color Doppler Imaging Study

Dear Eugenio Picano:

Thank you for your email of February 19, 2015, regarding our manuscript, “Severity of Aortic Regurgitation Assessed by Area of Vena Contracta: a Clinical Two-Dimensional and Three-Dimensional Color Doppler Imaging Study”, and the valuable comments of the two reviewers. I attach here our revised manuscript, as well as a point-by-point response to the reviewers’ comments.

We feel that the revised manuscript is a suitable response to the comments, and is significantly improved over the initial submission. We trust that it is now suitable for publication in the Cardiovascular Ultrasound.

Thank you in advance for your kind consideration of this paper.

Sincerely yours,

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Responses to the comments of Reviewer #1 (Julien Magne)

We wish to express our appreciation to the reviewer for their insightful comments on our paper. The comments have helped us significantly improve the paper.

1. For each number of patients reported, please add the related percentage.
Response: In accordance with the Reviewer’s comment, we have added the related percentage, “…52 of 61 patients (85.2%)” in page 2 (Abstract), line 13 and in page 7, line 3 (Results).

2. The CI may be added to area under the curve.
Response: In accordance with the Reviewer’s comment, we have added the 95%CI. We have performed statistical re-analysis of ROC curve with R (The R Foundation for Statistical Computing, Vienna, Austria) and we have also performed ROC curve analysis of 3DVCA. We have changed this text to: “The optimal 2DVCA cut-off for grading AR severity was 34 mm² (area under the curve: 0.95; 95% CI: 0.88-1; sensitivity: 78%; specificity: 95%) and the optimal 3DVCA cut-off for grading AR severity was 32 mm² (area under the curve: 0.96; 95% CI: 0.88-1; sensitivity: 89%; specificity: 98%); for reference, EROA was >30 mm² [3,4]. “, in page 7, line 12. We have added “and R (The R Foundation for Statistical Computing, Vienna, Austria) ”, in page 6, line 4 (Methods).

3. Regarding intra- and interobserver variability, please add SD.
Response: In accordance with the Reviewer’s comment, we have added SD, “intraobserver variability was 15.9±13.2%.” in page 8, line 1, and “interobserver variability was 14.8±13.5%.” in page 8, line 5.

Responses to the comments of Reviewer #2 (Stefano Nistri)

We wish to express our appreciation to the reviewer for their insightful comments on our paper. The comments have helped us significantly improve the paper.

1. General characteristics of patients should be better described (e.g.: LV volumes and diameters. EF, severity of AR, etc etc).
Response: In accordance with the Reviewer’s comment, we have added LV volume, diastolic diameter and EF, “Standard measurements were performed according to American Society of Echocardiography guidelines.” in page 5, line 7 (Methods) and “Left ventricular diastolic diameter was 52.0±8.1 mm, left ventricular end-diastolic volume was 134.7±53.0 mL, left ventricular ejection fraction was 52.9±10.8 % and 11 of 52 patients (21%) were severe aortic
regurgitation (EROA>30mm2).” in page 7, line 5 (Results).

2. The threshold of velocity range (65 cm/s) is it consistent with guidelines? Why has it been chosen? Please clarify.

Response: Several guidelines recommend the two dimensional measurement of color jet width with velocity range (Nyquist setting) of 50-60cm/sec. Nanda and colleagues reported that three dimensional vena contracta measurements was relatively constant with velocity range of 43-69 cm/sec, and Nozaki et al set the Nyquist velocity within 50-80 cm/sec. Lower velocity range results in an increased lowest velocity displayed on the color map, and an increased color flow jet area. We set the velocity range of > 65 cm/sec, to distinguish the high velocity regurgitant jet from the surrounding low velocity flow, especially for eccentric flow cases. In accordance with the Reviewer’s comment, we have changed from “Velocity range was >65 cm/s.” to “The Nyquist limit should be maximized to distinguish the high velocity regurgitant jet from the surrounding low velocity flow, especially for eccentric flow cases [6,7]. We set the velocity range at >65 cm/sec for clear visualization of high velocity flow of vena contracta [11,12,15].” in page 5, line 13. We have also added the following reference. “15. Nozaki S, Mizushige K, Taminato T, Obayashi N, Matsuo H, New Index for Grading the Severity of Aortic Regurgitation Based on the Cross-Sectional Area of Vena Contracta Measured by Color Doppler Flow Mapping. Circ J 2003; 67: 243 – 247.” in page 15, line 7 (References).

3. Please add in methods methodology for obtaining ERO.

Response: In accordance with the Reviewer’s comment, we have added “…EROA (calculated by the PISA method).” in page 5, line 8.

4. The issue of eccentricity has been considered in discussion: I’d suggest to separate with different symbols these patients in graphs and better describe the way to manage this common problem.

Response: In accordance with the Reviewer’s comment, we have added the Figure 6. In all 6 patients with eccentric AR, AR was severe (EROA>30mm2). VCW was >60mm in 3 of 6 (50%) patients, 2DVCA was >34mm2 in 5 of 6 (83%) and 3DVCA was >32mm2 in all 6 patients (100%). We have added “Figure 6. AR eccentricity affects accuracy of VCW, 2DVCA and 3DVCA. Relationship between EROA and VCW (left), 2DVCA (middle) and 3DVCA (right) for eccentric AR (red) and central AR (blue).” in page 21, line 9 (Figure legends), and “Fig. 6 shows the relationship between EROA and VCW (left), 2DVCA (middle) and 3DVCA. All 6 patients with eccentric AR (red) had severe AR (EROA>30mm2). VCW was >60mm in 3 of 6 (50%) patients with eccentric AR, 2DVCA was >34mm2 in 5 of 6 (83%) patients with eccentric AR and 3DVCA was >32mm2 in all 6 (100%) patients with eccentric AR. The measurement of the 2D or 3DVCA could be a useful and accurate method in patients with eccentric AR.” in page 10, line 7 (Discussion).
5. Moreover, the problems related to the difficulty to obtain a perpendicular image of the aortic valve (particularly in the elderly) should be more extensively debated.

Response: In accordance with the Reviewer’s comment, we have added “ in older patients with reduced aortoseptal angle and in patients with eccentric AR,” in page 9, line 1, and “In patients with calcified aortic valve lesion with eccentric AR jet, the measurement of 2DVCA may be inaccurate when valve calcification causes shadows or reverberations from parasternal window, and the measurement of 3DVCA from apical window is needed. The parasternal window provides superior axial resolution and the image from apical window is dependent on the lesser lateral resolution. In this clinical study, we used zoom mode with narrow sector angle and there was no significant difference between the measurements from either windows.” in page 9, line 2.

6. Comparison with precedent studies on the same topic could be interesting.

Response: In accordance with the Reviewer’s comment, we have added “The cut-off values for grading AR severity have been proposed: Fang et al have proposed 3DVCA >60 mm2 to define severe AR [11]. Chin et al reported that the cut-off value of 3DVCA was >50 mm2 for predicting severe AR [12]. Nozaki et al reported that 2DERO > 30 mm2 corresponded to severe aortic regurgitation [15]. In patients with central AR, if a circular configuration of the VCA is assumed, then VCA was calculated by using the VCW from the following formula: VCA= # x (VCW/2)2 . The VCW of 6mm correspond to VCA of 28.3 mm2, the VCW of 7 mm correspond to VCA of 38.5 mm2 and the VCW of 8 mm correspond to VCA of 50 mm2. The measurement of VCA can be affected the ultrasound machine, software and machine settings. In this study, we have reported that optimal cut-off value of 3DVCA was >32 mm2, 2DVCA was > 34 mm2, for reference, ERO was >30mm2. These thresholds need to be confirmed in further studies.” in page 9, line 2.

7. What about the potential role (if any) of the semiquantitative methods to solve the problems related to technical issues?.

Response: In accordance with the Reviewer’s comment, we have added “VCA can be measured simply by calculating the shape of regurgitant orifice as an ellipse, using the major (VCW1) and minor (VCW2) axis of the regurgitant flow, two orthogonal VCW: VCA= # x (VCW1)x (VCW2)/4, and this method may have a potential role as simple semiquantitative assessment of AR severity in patients with eccentric AR.” in page 10, line 7.