Prospective Comparison of Valve Regurgitation Quantitation by Cardiac Magnetic Resonance Imaging and Transthoracic Echocardiography

Cawley et al: Valve Regurgitation Quantitation

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Abstract

Background—Both transthoracic echocardiography (TTE) and cardiac magnetic resonance (CMR) imaging allow quantitation of chronic aortic (AR) and mitral regurgitation (MR). We hypothesized that CMR measurement of regurgitant volume (RVol) is more reproducible than TTE.

Methods and Results—TTE and CMR performed on the same day in 57 prospectively enrolled adults (31 AR, 26 MR) were measured by two independent physicians. TTE $RVol_{AR}$ was calculated as Doppler left ventricular (LV) outflow minus inflow stroke volume (SV). $RVol_{MR}$ was calculated by both the proximal isovelocity surface area (PISA) method and Doppler volume flow at 2 sites. CMR $RVol_{AR}$ was calculated by phase-contrast velocity mapping at the aortic sinuses and $RVol_{MR}$ as total LV minus forward SV. Intra- and interobserver variability were similar. For AR, Bland-Altman mean interobserver difference in RVol was -0.7 mL (95% CI -5 to 4 mL) for CMR and -9 mL (95% CI -53 to -36 mL) for TTE. Pearson correlation was higher ($p = 0.001$) between CMR (0.99) than TTE readers (0.89). For MR, Bland-Altman mean difference in RVol between observers was -4 mL (95% CI -21-13 mL) for CMR compared to 0.7 mL (95% CI -30-32 mL) for PISA and -10 mL (95% CI -76-56 mL) for TTE volume flow at 2 sites. Correlation was similar for CMR (0.94) versus TTE readers (0.90 for PISA).

Conclusions—Compared to TTE, CMR has lower intra- and interobserver variability for $RVol_{AR}$ suggesting CMR may be superior for serial measurements. Although $RVol_{MR}$ is similar by TTE and CMR, variability in measured RVol by both approaches suggests caution is needed in clinical practice.

Key Words: regurgitation, valves, mitral valve, magnetic resonance imaging, echocardiography

Transthoracic echocardiography (TTE) is the standard clinical tool for initial assessment and longitudinal evaluation of patients with valvular heart disease [1]. Current clinical guidelines for management of adults with chronic valve regurgitation include clear recommendations for measuring regurgitant severity.[1, 2] Quantitation is recommended as a tool to identify patients at risk of adverse long-term physiologic consequences, including irreversible left ventricular (LV) contractile dysfunction, and to prevent adverse clinical outcomes, including heart failure, sudden death and cardiovascular mortality.

TTE allows measurement of regurgitant volume, fraction and orifice area and has been well validated both in both experimental and clinical studies.[2] In addition, regurgitant orifice area has been shown to be predictive of clinical outcome for both aortic (AR) and mitral regurgitation (MR).[3] However, echocardiographic quantitation of valve regurgitation can be challenging due to poor acoustic windows, dynamic or eccentric jets, and geometric assumptions.[2, 4, 5]

Cardiovascular magnetic resonance imaging (CMR) is an alternative modality for assessing patients with chronic valve regurgitation based on measurement of LV volumes and phase contrast velocity mapping.[6-8] CMR has several potential advantages compared to TTE including improved endocardial definition, fewer geometric assumptions, and less angle dependence for flow measurements. However there is little data on direct systematic comparisons, including reproducibility, between TTE and CMR for quantitation of AR and MR. Thus, we hypothesized that CMR has less interobserver variability when quantifying chronic AR and MR and thus may be preferable for longitudinal followup in individual patients.

Methods

Study Population

We prospectively enrolled 57 adults with *either* chronic AR or MR to undergo quantitative TTE and CMR on the same day from January 2008 to July 2010. Subjects were identified from the University of Washington Echocardiography Lab, Harborview Medical Center Echocardiography Lab, and cardiology or cardiac surgery outpatient clinics at either institution. Exclusion criteria were more than mild regurgitation of a second valve, atrial fibrillation at the time of imaging, known poor acoustic windows, extreme claustrophobia, and non-CMR compatible implanted devices. All patients gave written informed consent and the study was approved by the University of Washington Institutional Review Board.

Echocardiography

TTE was performed using a commercially available system (Acuson Sequoia CS 12 system; Siemens Medical Solutions, USA) with two-dimensional imaging and Doppler data recorded using a 4V1c multi-Hertz transducer and dedicated continuous wave (CW) Doppler transducer (2MHz). Subjects were scanned in the left lateral decubitus position with digital recording of standard image planes and Doppler data. For both TTE and CMR, total stroke volume (TSV) was defined as the total volume of blood ejected by the LV in systole, which includes both the regurgitant volume (RVol) and the forward stroke volume (FSV) delivered to the systemic circulation.

Quantitation of Regurgitation: RVol was quantitated by measuring transvalvular antegrade stroke volumes (SV) at the LV outflow tract (LVOT) and mitral annulus (MA) as shown in Figure 1.[2] For MR, RVol also was calculated using total LV stroke volume calculated from the

apical biplane 2D approach (LV-SV_{2D}) as shown in Figure 1. The proximal isovelocity surface area (PISA) method for calculation of mitral regurgitant orifice area (ROA) and RVol as shown in Figure 2 also was used. [2]

LV Volumes: LV volumes were calculated with the standard apical biplane formula from TTE apical four-chamber and two-chamber views with tracing of endocardial borders at end-diastole and end-systole. Care was taken to avoid apical foreshortening and to optimize endocardial definition by use of harmonic imaging and adjustment of other instrument settings.

CMR Imaging

CMR images were acquired the same day as the TTE images on a commercially available 1.5-Tesla system (Achieva; Philips Medical, Best, The Netherlands). A standard body coil was used for radio frequency transmission and a dedicated 5 channel phased array cardiac receiver coil was used for reception. Retrospective ECG gating was used for all techniques. Breath-held through-plane phase contrast flow imaging was performed at the level of the sinuses of using 45 phases per R-R interval with the following representative scan parameters: repetition time (TR), 4.3 ms; echo time (TE), 2.6 ms; flip angle, 15º; number of averages 2, SENSE factor 2, temporal resolution, 17 ms for an example heart rate of 80 bpm; in-plane spatial resolution, 2.5 x 2.5 mm; slice thickness 6 mm; scan time approximately 16-18 s without background correction. A maximum velocity (v_{enc}) was encoded into the sequence, starting at 200 cm/second. If aliasing occurred, then the maximum velocity was increased by 50 cm/second until aliasing did not occur.

LV volumes were measured by tracing endocardial borders on stack of short axis images obtained from breath-held steady-state free- precession (SSFP) covering the entire left ventricle,

from base to apex, 1 slice/breath-hold. Papillary muscles and trabeculations were included in the blood pool on the contours. The 3 long axis cines (2CH, 3CH, 4CH) were carefully viewed using a cross-plane localizer to select the most basal and apical slices to include in the LV volumes. End-diastolic (EDV) and end-systolic volumes (ESV) calculated by summation of disks. TSV was calculated as: TSV = EDV –ESV. *CMR assessment of RVol based on subtracting right ventricular SV from LV SV is described in the Supplement.*

Aortic phase contrast velocity mapping was used to calculate AR RVol from the area under the retrograde diastolic flow curve recorded at the sinuses (Figure 3).[9, 10] TSV was measured as the area under the antegrade systolic flow curve.

MR regurgitant volume ($RVol_{MR}$) was calculated by subtracting the aortic valve FSV ($FSV_{aortic\ flow}$) measured by phase-contrast velocity mapping from TSV ($TSV_{LV\ volumes}$) measured by the volumetric imaging method: $RVol_{MR} = TSV_{LV\ volumes} - FSV_{aortic\ flow}$.

Data Measurements and Statistical Analysis

TTE measurements were made by two experienced observers (CMO, PJC) blinded to all other TTE and CMR measurements using a Syngo Dynamics Workspace (V5.05, Siemens Medical Solutions, Malvern, PA). Similarly blinded CMR measurements were made by two experienced physicians (PJC, CHC) using a commercial analysis platform (Extended MR Workspace v2.6.1; Philips Healthcare, Best, The Netherlands). Study images were identified by a coded study number. Intraobserver variability for TTE (CMO) and CMR (CHC) was assessed by repeating measurements several months after initial readings. Based on *a priori* power calculations, a total of n=10 AR studies and n=10 MR studies were repeated.

Baseline characteristics are reported as descriptive statistics, with means, standard deviations and ranges. Categorical outcomes are presented as counts and percentages. As specified *a priori*, analyses were stratified by site of valve regurgitation (aortic or mitral), though measurements performed in both groups were combined to increase statistical power. Interobserver variability for TTE (PJC vs. CMO) and CMR (PJC vs. CHC) were determined for each measure, using Bland-Altman and linear regression analyses, calculation of mean difference, two-sided 95% limits of agreement and Pearson's correlation coefficient. Bootstrapping methods were used to assess differences between dependent correlation coefficients. The coefficient of variation (CV) was calculated based on within-subject variance using the equation:

$$CV = 100\% * \sqrt{((\sum (((M2 - M1)\text{^}2/2)) / (((M2 + M1)/2)\text{^}2\ ))/N)}$$

Where M1= observer 1 measurement, M2 = observer 2 measurement, and N= number of measurement pairs. Intermodality (TTE vs. CMR for reader PJC) and intraobserver variability were determined using similar methods. Intermodality agreement was assessed using Student t-tests for dependent variables

Sample size calculations (see appendix for additional details) were performed for each group using the measurement error (=100%*√[within-patient variance]/mean (all measurements))as an estimate of the standard deviation in outcome variables. Statistical analyses were performed using Stata/IC 11.2 for Windows (StataCorp LP, College Station TX). Presented p-values are two-sided, with significance threshold of $p<0.05$.

Results

Study Population: Baseline characteristics of the study population are shown in Table 1. Mitral RVol ranged from 2.6 to 123 mL (mean 39±33 mL) by the Doppler PISA method and from 9 to 97 mL (mean 42±25 mL) by CMR. Mitral ROA by the PISA method ranged from 0.03 to 0.76 cm^2 (mean 0.26±0.20 cm^2). Aortic RVol ranged from -12 to 178 mL (mean 62±45 mL) by Doppler echocardiography and from 6.5 to 140 mL (mean 52±37 mL) by CMR.

Intraobserver variability: Intraobserver variability is shown in Table 2. CMR measurements showed little variability with a mean difference near zero, narrow limits of agreement and a correlation coefficient close to one for all measurements. Echocardiography measurements showed greater variability based on Bland-Altman analysis. Correlation coefficients for repeat CMR measurements were significantly higher than TTE measurement for LV ejection fraction, LV end diastolic volume, transaortic stroke volume, and aortic RVol.

Interobserver variability*:* The interobserver variability for aortic and mitral regurgitant volumes, based on repeat measurements of recorded images, is summarized in Table 3 and graphically depicted in Figures 4 & 5. Data are similar for regurgitant fraction (not shown). In general, the CMR phased contrast velocity method showed lower variability than the CMR RV-LV volume method (see Supplement).

For aortic regurgitation, the mean difference and limits of agreement in measurements between observers were greater for TTE than CMR. In addition, linear correlation between measurements was better for CMR measurements ($P \leq 0.005$)

For mitral regurgitation, the volume flow at two sites approach had wider limits of agreement than the PISA or LV volumes approaches. In addition, the PISA approach showed a higher linear correlation coefficient than the other 2 methods. Compared to any of the TTE

approaches, CMR regurgitation volume had narrower limits of agreement and a higher Pearson correlation coefficient, but these differences did not reach statistical significance. Interobserver variability for TTE assessment of vena contracta or regurgitant orifice area showed no mean difference between readers but the limits of agreement were wide compared to the classification of disease severity.

Measurement of LV volumes and ejection fraction by echocardiography consistently showed a greater mean difference and wider limits of agreement compared to CMR (Table 3). Although, measurement of transaortic volume flow rate by Doppler showed less measurement variability than LV volumes and ejection fraction, the limits of agreement were still wider than the CMR phase contrast velocity mapping approach. (Figures 6 & 7)

Comparison of TTE and CMR: The primary purpose of this study was to examine intra- and interobserver measurement variability but intermodality comparison of TTE and CMR measures of regurgitant severity also provides some useful insights. Although, TTE and CMR regurgitant volumes correlated moderately well with each other for both aortic and mitral regurgitation (Table 4) with a linear regression line near the line of identify, there was considerable scatter of the data across the range of regurgitant volume (Figure 8). LV volumes were consistently underestimated by TTE compared to CMR ($P<0.00005$). Doppler transaortic flow compared well to CMR transaortic phase contrast velocity mapping although there was a relative overestimation at higher flow rates by the Doppler approach.

Improvements in inter-observer variability can enhance clinical trials by reducing the sample size required to achieve similar statistical power. For a hypothetical study examining aortic regurgitant volume, with an expected treatment effect of a 20% reduction in regurgitation, the required sample size to obtain 80% power at a $p=0.05$ level would be n=48 for TTE and n=6

for CMR. A similar study of mitral regurgitant volume would require n=60 using the TTE PISA method, n=82 using the TTE Doppler at 2 sites method, and n=198 for the TTE 2D volume method, but only n=26 using CMR.

Discussion

The results of this prospective direct comparison of TTE and CMR quantitation of aortic and mitral regurgitant severity confirmed our hypothesis that CMR has less intraobserver and interobserver variability than TTE as judged by higher correlation coefficients, smaller mean differences and narrower limits of agreements for measurements made by experienced physicians. Our data are representative of clinical practice with patient characteristics, causes of valve dysfunction and severity range typical for adults with chronic regurgitation. This is the first study to directly compare intra- and interobserver measurement variability for CMR and TTE quantitation of AR and MR severity in the same patients studied on the same day.

Echocardiography: TTE measures of regurgitant severity are important for clinical decision making both for recommendations about timing of sequential monitoring and for optimal timing of surgical intervention. TTE can easily separate mild from severe regurgitation using simple measures such as vena contracta width and continuous wave Doppler. However, precise measurement of regurgitant volume is more challenging.

For AR, a PISA often is poorly visualized so that quantitation requires measurement of total SV across the aortic valve and forward SV across a non-regurgitant valve. We found good reproducibility for transaortic SV measurements, including the separate components of LV outflow diameter and velocity time integral. In contrast, there was wide variability for measurement of transmitral annular diameter and velocity time integral. These data are

congruent with older TTE studies using volume flow quantitation in measurement of aortic stenosis and valve regurgitation.[11-14]

Precise and reproducible measurement of mitral annulus diameter is difficult on TTE due to its noncircular nonplanar 3D shape. In addition, measuring diameter and velocity at the same anatomic site is challenging because a parasternal diameter measurement may not match the apical Doppler sample volume location, resulting in over or underestimation of the flow area. Mitral annular measurements from the apical window can be spatially matched to sample volume location but beam width at this depth limits accuracy. In contrast, TTE parasternal aortic annular diameter measured at the aortic leaflet insertion points can be spatially matched to the Doppler recording based on the presence of an aortic valve closing click which likely accounts for the high reproducibility of TTE transaortic stroke volume calculations.

MR can be measured on TTE using several different approaches. As with AR, we found considerable variability in calculations based on the volume flow at 2 sites method. Again, variability was due to mitral annular and transmitral velocity measurements. Substitution of the total stroke volume derived from 2D biplane apical LV volumes for transmitral flow did not reduce variability because of the significant variability in TTE measurements of LV volumes.

Of the three TTE methods evaluated, the PISA approach showed the best reproducibility for MR quantitation. There was a low interobserver variability for both the PISA diameter measurement (r= 0.91) and the continuous wave Doppler MR jet peak velocity (r=0.85) and velocity time integral (r=0.95).[5] Reproducibility was similar for central and eccentric jets as well as for holosystolic and late systolic regurgitation. We traced only the recorded continuous wave Doppler jet because of lack of agreement in extrapolating a holosystolic curve. However, data

are similar if regurgitation is assumed to be holosystolic and a curve is extrapolated to the "missing" part of the flow curve.

Cardiac magnetic resonance imaging; Intra and inter-observer variability for CMR measurement of aortic regurgitant fraction showed only a small mean difference, narrow limits of agreement and a high correlation coefficient that was significantly better than the correlation for TTE measurement of regurgitant volume. [15] The key factors that ensure reproducibility of phase contrast velocity measurements include correct alignment of the region of interest at the level of the aortic sinuses and careful selection of the flow area.[16, 17] Measurements made at the valve level are less reproducible due to turbulence and to movement of the valve plane into and out of the image plane during the cardiac cycle. Recording more distally in the ascending aorta results in reduced sensitivity for detecting regurgitation, presumably due to vascular recoil, resulting in falsely low regurgitant volumes. In clinical practice, the effect of different scanner platforms and background correction remains unknown.

CMR calculation of mitral regurgitant volume relied on two measurements—forward stroke volume measured by phase contrast in the aorta and total LV stroke volume calculated from endocardial border tracings. Thus CMR mitral regurgitant volume showed more intra- and interobserver variability than CMR aortic regurgitant volume. Even so, there was a trend towards better reproducibility for MR severity by CMR compared to any of the TTE approaches, although this difference did not reach statistical significance. CMR calculation of RVol based on the different between RV and LV stroke volumes derived from endocardial border tracings were slightly more variable than phase contrast and LV volume measurements, due to the combined variability of measuring left and right ventricular volumes (See Supplement). [8]

Comparison between modalities: In the absence of an external reference standard for regurgitant volume, the accuracy of CMR versus TTE measurements cannot be assessed in this study. However, we expected these modalities to correlate with each other, based on the assumption that both approaches are measuring the same physiologic parameters and both have previously been independently validated compared to reference standards .[8, 16-18] In addition, echocardiographic PISA calculation of regurgitant orifice area and CMR measurement of AR regurgitant fraction both have established prognostic value.[19, 20]

Our data show that measurement of LV volumes and ejection fraction by CMR is more reproducible than by 2D TTE. Previous studies have shown that CMR is more accurate than TTE for LV volume determination and, as found in previous studies, we similarly found that TTE consistently underestimates LV volumes and overestimates ejection fraction compared to CMR. Underestimation of LV volumes by TTE is due to three factors. First, even with optimal TTE image acquisition, apical views often are foreshortened because the ultrasound window does not allow access to the true LV apex. Second, echocardiographic endocardial borders reflect the inner edge of LV trabeculations whereas CMR borders indicate the compacted myocardial border. Third, TTE volume calculation use geometric formulas whose assumptions about LV shape may not be valid, particularly with the increased LV sphericity seen with chronic aortic regurgitation. Echocardiographic measurement variability and underestimation of LV volumes may have important clinical implications if TTE results in underestimation of regurgitant severity or fails to recognize early LV systolic dysfunction in patients with chronic regurgitation.

In contrast, TTE Doppler measurement of transaortic volume flow rate correlates reasonably well with CMR transaortic systolic flow by the phase contrast velocity methods.

Given these findings, measurement of noninvasive cardiac output by TTE should be considered more widely in clinical practice.[21]

Study limitations: This study has several limitations. First we only examined intra- and interobserver variability in measurements, as it was impractical to repeat the TTE and CMR studies to assess test-retest reproducibility. Physiologic variability in loading conditions may confound comparison of serial studies in clinical practice. Second, there is no precise reference standard for clinical measurement of regurgitant volume, and TTE and CMR were compared directly. However, these methods have been well validated in research models. Third, our study aim was to evaluate currently available standard clinical measurements. We did not perform phase contrast velocity mapping across the mitral annulus because of difficulty defining an annular plane and apical motion of the annulus during the cardiac cycle. TTE methods did not include 3D measurement of LV volumes or 3D color visualization of proximal jet geometry as these approaches were unavailable at our center at study onset. Some studies have suggested that vena contracta measurements on TTE are more reproducible than other measures [22] but other studies found considerable variability [23]. We did not evaluate vena contracta because it cannot be directly compared to CMR measurements. Finally, we cannot exclude the possibility that observed differences in interreader variability are due to reader effects, rather than true differences in methodology.

Clinical Implications: Quantitation of regurgitant severity in adults with chronic AR and MR is challenging. In the clinical setting, variability in recording and measuring data, along with physiologic variability, affects both the classification of disease as mild, moderate or severe and impacts our ability to detect changes in disease severity overtime. Echocardiography offers the advantages of widespread availability, lower cost and the ability to measure regurgitation

orifice area as well as regurgitant volume and fraction. However, even with optimal data acqusition, there is considerable variability in these measurements. CMR regurgitant severity measures show less variability but this modality is not as widely available and, like TTE, requires meticulous data acquisition and analysis by experienced physicians for accurate results.

These variability data highlight the need for caution in defining chronic regurgitation as "severe" based on a single TTE or CMR measurement of regurgitant volume or regurgitant fraction. CMR quantitation of AR severity may be helpful in cases where the degree of LV enlargement is greater than expected based on TTE measures of regurgitation in order to determine if LV dilation is likely due to chronic AR. CMR also is appropriate when more accurate and reproducible measurement of LV volumes or ejection fraction is needed for optimal timing of mechanical intervention. For clinical trials, the more accurate and reproducible regurgitant severity and LV volumes data provided by CMR might allow a smaller study size for evaluation of medical therapy and for determining more precisely the optional LV volume break-points for timing of valve intervention.

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Disclosures

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References

1. Bonow RO, Carabello BA, Kanu C, de Leon ACJ, Faxon DP, Freed MD, Gaasch WH, Lytle BW, Nishimura RA, O'Gara PT, O'Rourke RA, Otto CM, Shah PM, Shanewise JS, Smith SC, Jr., Jacobs AK, Adams CD, Anderson JL, Antman EM, Faxon DP, Fuster V, Halperin JL, Hiratzka LF, Hunt SA, Lytle BW, Nishimura R, Page RL, Riegel B. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease. *Circulation.* 2006;114:e84-231.
2. Zoghbi WA, Enriquez-Sarano M, Foster E, Grayburn PA, Kraft CD, Levine RA, Nihoyannopoulos P, Otto CM, Quinones MA, Rakowski H, Stewart WJ, Waggoner A, Weissman NJ. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. *J Am Soc Echocardiogr.* 2003;16:777-802.
3. Enriquez-Sarano M, Avierinos JF, Messika-Zeitoun D, Detaint D, Capps M, Nkomo V, Scott C, Schaff HV, Tajik AJ. Quantitative determinants of the outcome of asymptomatic mitral regurgitation. *N Engl J Med.* 2005;352:875-83.
4. Buck T, Plicht B, Kahlert P, Schenk IM, Hunold P, Erbel R. Effect of dynamic flow rate and orifice area on mitral regurgitant stroke volume quantification using the proximal isovelocity surface area method. *J Am Coll Cardiol.* 2008;52:767-78.
5. Foster E, Wasserman HS, Gray W, Homma S, Di Tullio MR, Rodriguez L, Stewart WJ, Whitlow P, Block P, Martin R, Merlino J, Herrmann HC, Wiegers SE, Silvestry FE, Hamilton A, Zunamon A, Kraybill K, Gerber IL, Weeks SG, Zhang Y, Feldman T. Quantitative assessment of severity of mitral regurgitation by serial echocardiography in a multicenter clinical trial of percutaneous mitral valve repair. *Am J Cardiol.* 2007;100:1577-83.
6. Kon MW, Myerson SG, Moat NE, Pennell DJ. Quantification of regurgitant fraction in mitral regurgitation by cardiovascular magnetic resonance: comparison of techniques. *J Heart Valve Dis. 2004*; 13:600-7.
7. Ley S, Eichhorn J, Ley-Zaporozhan J, Ulmer H, Schenk JP, Kauczor HU, Arnold R. Evaluation of aortic regurgitation in congenital heart disease: value of MR imaging in comparison to echocardiography. *Pediatr Radio.* 2007;37:426-36.
8. Cawley PJ, Maki JH, Otto CM. Cardiovascular magnetic resonance imaging for valvular heart disease: technique and validation. *Circulation.* 2009;119:468-78.
9. Chatzimavroudis GP, Walker PG, Oshinski JN, Franch RH, Pettigrew RI, Yoganathan AP. Slice location dependence of aortic regurgitation measurements with MR phase velocity mapping. *Magn Reson Med.* 1997;37:545-51.

10. Chatzimavroudis GP, Oshinski JN, Pettigrew RI, Walker PG, Franch RH, Yoganathan AP. Quantification of mitral regurgitation with MR phase-velocity mapping using a control volume method. *J Magn Reson Imaging.* 1998;8:577-82.
11. Otto CM, Pearlman AS, Comess KA, Reamer RP, Janko CL, Huntsman LL. Determination of the stenotic aortic valve area in adults using Doppler echocardiography. *J Am Coll Cardiol.* 1986;7:509-17.
12. Otto CM, Pearlman AS, Gardner CL, Enomoto DM, Togo T, Tsuboi H, Ivey TD. Experimental validation of Doppler echocardiographic measurement of volume flow through the stenotic aortic valve. *Circulation.* 1988;78:435-41.
13. Otto CM, Nishimura RA, Davis KB, Kisslo KB, Bashore TM, Balloon Valvuloplasty Registry Echocardiographers. Doppler echocardiographic findings in adults with severe symptomatic valvular aortic stenosis. *Am J Cardiol.* 1991;68:1477-84.
14. Lewis Jf, Kuo LC, Nelson JG, Limacher MC, Quinones MA. Pulsed Doppler echocardiographic determination of stroke volume and cardiac output: clinical validation of two methods using the apical window. *Circulation.* 1984;70:425-31.
15. Dulce MC, Mostbeck GH, O'Sullivan M, Cheitlin M, Caputo GR, Higgins CB. Severity of aortic regurgitation: interstudy reproducibility of measurements with velocity-encoded cine MR imaging. *Radiology.* 1992;185:235-40.
16. Hundley WG, Li HF, Willard JE, Landau C, Lange RA, Meshack BM, Hillis LD, Peshock RM. Magnetic resonance imaging assessment of the severity of mitral regurgitation. Comparison with invasive techniques. *Circulation.* 1995;92:1151-8.
17. Fujita N, Chazouilleres AF, Hartiala JJ, O'Sullivan M, Heidenreich P, Kaplan JD, Sakuma H, Foster E, Caputo GR, Higgins CB. Quantification of mitral regurgitation by velocity-encoded cine nuclear magnetic resonance imaging. *J Am Coll Cardiol.* 1994;23:951-8.
18. Kizilbash AM, Hundley WG, Willett DL, Franco F, Peshock RM, Grayburn PA. Comparison of quantitative Doppler with magnetic resonance imaging for assessment of the severity of mitral regurgitation. *Am J Cardiol.* 1998;81:792-5.
19. Detaint D, Messika-Zeitoun D, Maalouf J, Tribouilloy C, Mahoney DW, Tajik AJ, Enriquez-Sarano M. Quantitative echocardiographic determinants of clinical outcome in asymptomatic patients with aortic regurgitation: a prospective study. *JACC Cardiovasc Imaging.* 2008;1:1-11.
20. Myerson SG, d'Arcy J, Mohiaddin R, Greenwood JP, Karamitsos TD, Francis JM, Banning AP, Christiansen JP, Neubauer S. Aortic regurgitation quantification using cardiovascular magnetic resonance: association with clinical outcome. *Circulation.* 2012;126:1452-60
21. Lancellotti P, Pierard LA, Voigt JU, Miller O, Nieman K, Rademakers FE, Badano LP. EuroEcho and other imaging modalities: highlights. *Eur Heart J Cardiovasc Imaging.* 2012;13:127-31.
22. Roberts BJ, Grayburn PA. Color flow imaging of the vena contracta in mitral regurgitation: technical considerations. *J Am Soc Echocardiogr.* 2003;16:1002-6.
23. Biner S, Rafique A, Rafii F, Tolstrup K, Noorani O, Shiota T, Gurudevan S, Siegel RJ. Reproducibility of proximal isovelocity surface area, vena contracta, and regurgitant jet area for assessment of mitral regurgitation severity. *JACC Cardiovasc Imaging.* 2010;3:235-43.

Table 1. Baseline Study Population

	Mean±SD	Range
Mitral Regurgitation (N=26)		
Age(years)	54±13	29-77
Female, N (%)	11(42%)	
Causes of MR		
Myxomatous	24(92%)	
Ischemic	1(4%)	
Endocarditis	1(4%)	
Height(cm)	176±11	152-193
Weight(kg)	74±13	45-103
Body surface area(m^2)	1.90±0.21	1.39–2.34
Systolic BP(mmHg)	123 ± 13	95 -152
Diastolic BP(mmHg)	71 ± 8	49 - 82
Pulse Pressure(mmHg)	52 ± 12	32 -80
Aortic Regurgitation (N=31)		
Age(years)	47±13.5	24-77
Female, N(%)	4 (13%)	
Causes of AR		
Bicuspid valve	19(61%)	
Aortic aneurysm	6(19%)	
Endocarditis	2(6%)	
Rheumatic	1 (3%)	
Other	3(10%)	
Height(cm)	177±10	150-196
Weight(kg)	88±17	58-123
Body surface area(m^2)	2.06±0.22	1.53-2.54
Systolic BP(mmHg)	126±15	102-160
Diastolic BP(mmHg)	65±12	36-86
Pulse Pressure(mmHg)	62±17	33-110

AR, aortic regurgitation; BP, blood pressure; MR, mitral regurgitation

Table 2. Intra-observer measurement variability

	TTE			CMR		
	Bland-Altman*	r-value**	CV (%)	Bland-Altman*	r-value**	CV (%)
Aortic regurgitation(n=10)						
Regurgitant volume(mL)	3(-38 to 45)	0.92	32.1	0(-2 to 2)	0.99^	3.8
Regurgitant fraction(%)	3(-24 to 30)	0.87	31.4	0(-2 to 2)	0.99	3.3
Vena contracta(mm)	-0.1(-0.5 to 0.3)	0.87	16.8			
Mitral regurgitation (n=10)						
Regurgitant volume (mL)				0(-18 to 17)	0.96	25.9
PISA	-4(-29 to 22)	0.96	29.1			
Volume flow 2 sites	21(-28 to 72)	0.85	36.5			
2D LV + Doppler	6(-33 to 46)	0.93	84.5			
Vena contracta(mm)	-0.1(-0.3 to 0.1)	0.90	16.5			
ROA(cm^2)	0(-0.2 to 0.2)	0.97	25.1			
Left ventricle (n=20)						
End-diastolic volume(mL)	3(-38 to 44)	0.88	9.1	-0(-16 to 17)	0.99^^	3.3
End-systolic volume(mL)	4(-11 to 18)	0.91	9.8	1(-18 to 20)	0.95	9.0
Stroke volume(mL)	-1(-34 to 32)	0.85	11.9	-1(-14 to 12)	0.98	4.9
Ejection fraction(%)	-2(-9 to 5)	0.87	4.6	0(-5 to 4)	0.92^^	2.7
Transaortic systolic flow (n=20)						
Doppler LVOT(mL)	-7(-27 to 12)	0.98	8.8			
CMR phase contrast velocity mapping (mL)				0(-2 to 2)	0.99^	2.0

* Mean difference (two-sided 95% confidence limits of agreement)
** Pearson Correlation (all p-values < 0.00005)
^^ p < 0.02 for CMR versus TTE r-value
^ p < 0.00005 for CMR versus TTE r-value

CV, coefficient of variation; 2D LV, left ventricular volumes measured from two dimensional echocardiography; LVOT, left ventricular outflow tact; PISA, proximal isovelocity surface area approach; ROA, regurgitant orifice area.

Table 3. Inter-observer measurement variability

	TTE			CMR			TTE vs CMR
	Bland-Altman*	r-value**	CV (%)	Bland-Altman*	r-value**	CV	p-value^
Aortic regurgitation(n=31)							
Regurgitant volume(mL)	-9(-53 to 36)	0.89	52.4	-0.7 (-5 to 4)	0.99	5.2	0.005
Regurgitant fraction(%)	-4(-32 to 24)	0.84	51.6	-0.7 (-4 to 3)	0.99	6.1	0.007
Vena contracta(mm)	0.1(0.3-0.6)	0.72	23.9				
Mitral regurgitation (n=26)							
Regurgitant volume (mL)				-4 (-21 to 13)	0.94	20.4	
PISA	0.7(-30 to 32)	0.90	29.6				NS
Volume flow 2 sites	-10(-76 to 56)	0.86	35.4				NS
2D LV + Doppler	-0.4(-35 to 34)	0.84	97.2				NS
Vena contracta(mm)	0.07(-0.2 to 0.4)	0.68	20.0				
ROA(cm^2)	0(-0.19 to 0.21)	0.88	26.4				
Left ventricle (n=57)							
End-diastolic volume(mL)	-17(-54 to 20)	0.93	11.4	-2(-30 to 27)	0.98	4.1	0.01
End-systolic volume(mL)	-11(-30 to 8)	0.93	18.5	1(-16 to 17)	0.98	5.8	0.02
Stroke volume(mL)	-6(-39 to 27)	0.85	13.6	-3(-22 to 15)	0.97	5.2	0.005
Ejection fraction(%)	3(-9 to 14)	0.77	7.4	-1(-7 to 5)	0.91	3.4	0.03
Transaortic systolic flow (n=57)							
Doppler LVOT(mL)	-6(-27 to 14)	0.98					
CMR phase contrast flow(mL)				0(-6 to2)	0.99	2.8	0.01

* Mean difference (two-sided 95% confidence limits of agreement)
** Pearson Correlation (all p-values < 0.00005)
^p-value comparing TTE and CMR correlations
Abbreviations as in Table 2.

Table 4. CMR versus Echo Measurements

	TTE	CMR		
	Mean ± SD	Mean ±SD	t-test	r-value*
Aortic regurgitation(n=31)				
Regurgitant volume(mL)	62±45	52±37	0.11	0.64
Regurgitant fraction(%)	34±21	35±18	0.65	0.57
Vena contracta(mm)	5±2			
Mitral regurgitation (n=26)				
Regurgitant volume (mL)		42±25		
PISA	39±33		0.56	0.70
Volume flow 2 sites	79±61		0.0008	0.64
2D LV + Doppler	9±31		<0.0001	0.79
Vena contracta(mm)	5±2			
ROA(cm^2)	0.26±0.20			
Left ventricle (n=57)				
End-diastolic volume(mL)	166±48	243±69	<0.0001	0.91
End-systolic volume(mL)	64±26	103±37	<0.0005	0.87
Stroke volume(mL)	102±29	140±38	<0.0005	0.86
Ejection fraction(%)	62±8	58±7	<0.0005	0.64
Transaortic systolic flow (n=57)				
Doppler LVOT(mL)	127±55		0.0001	0.87
CMR phase contrast flow(mL)		111±39		

*p-value for all TTE-CMR correlation r-values is ≤ 0.0001

Figure Legends

Figure 1. TTE quantitation of MR volume. LV outflow tract (LVOT) diameter was measured at the aortic valve leaflet insertion points in mid systole to calculate a circular cross sectional area (CSA). LVOT velocity-time integral (VTI) was recorded from the apical window, with the sample volume just on the LV side of the aortic valve. Mitral annulus (MA) diameter (D) was measured from the apical 4 chamber view during early diastole (E wave). From an apical window, the Doppler sample volume positioned at the mitral annulus and modal velocity traced for the VTI. Stroke volume (SV at each site was used to calculate regurgitant volume (RVol) for aortic (AR) and mitral (MR) regurgitation as shown. Total stroke volume also was calculated from 2D LV volumes ($LV\text{-}SV_{2D}$).

Figure 2. Proximal isovelocity surface area (PISA) method for calculation of RVol and ROA. In the apical view that best demonstrated a PISA on color Doppler, the baseline was shifted in the direction of the regurgitant jet to obtain an aliasing velocity between 30 and 40 cm/s. A narrowed sector width and a shallower depth were used to optimize scan line density and frame rate. PISA radius (r) was measured from the aliasing velocity ($V_{aliasing}$) to the level of the valve orifice. The regurgitant jet was recorded with CW Doppler for measurement of maximum velocity (V_{MR}) and the velocity time integral (VTI_{MR}). For mitral regurgitant jets that were not pan-systolic, only the Doppler signal that represents mitral regurgitation was traced.

Figure 3. CMR measurement of transaortic phase contrast imaging. A slice orthogonal to aortic flow in two imaging planes (3 chamber and coronal aorta SSFP) was selected and positioned at

the aortic valve leaflet tips (about halfway between aortic annulus and sinotubular junction) as shown on the diastolic magnitude image (left). A region-of-interest (ROI) was outlined within the lumen of the aorta on each phase (45 in total) of the phase velocity map (center), with the resultant time velocity curve displayed on the right, the x-axis being the time in milliseconds from the ECG R-wave.

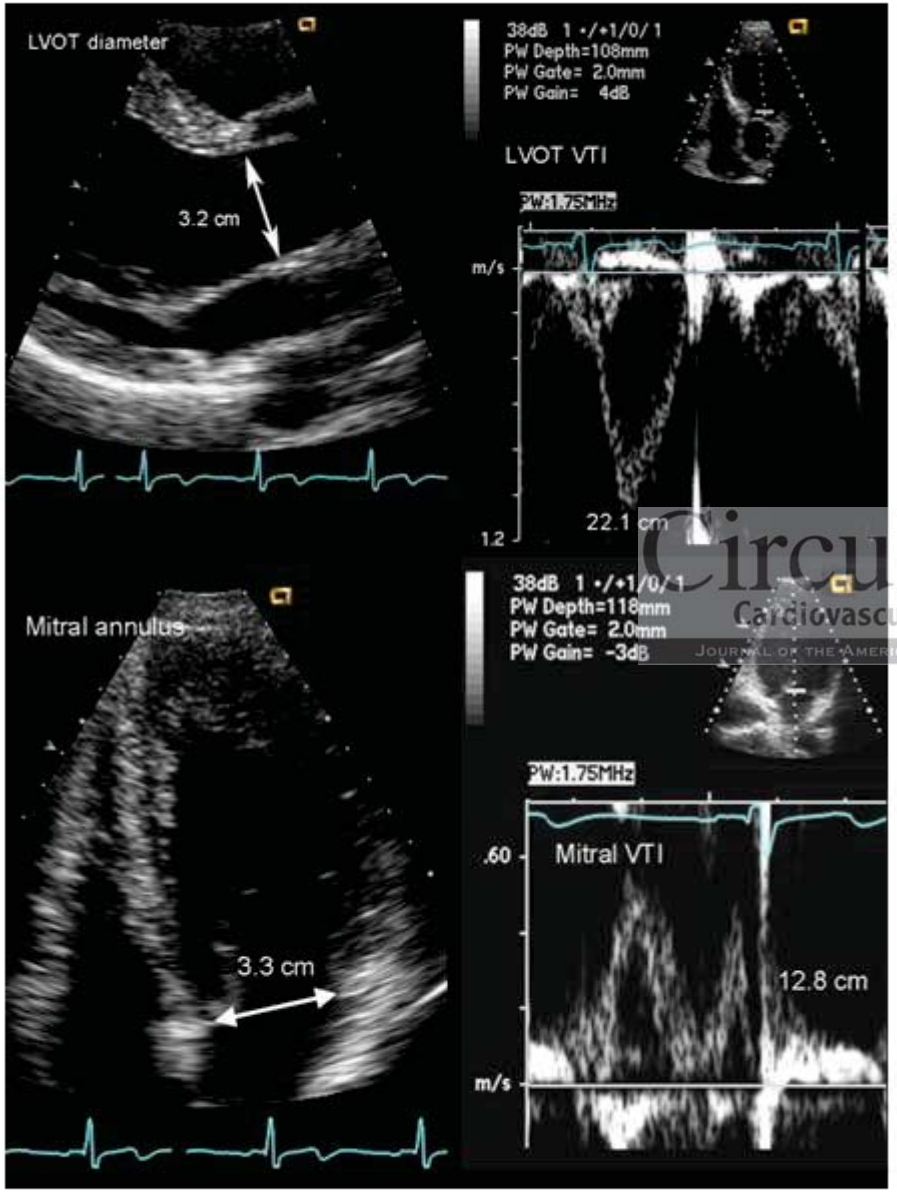
Figure 4. Linear regression (top) and Bland-Altman plots (bottom) for aortic regurgitant (AR) volume measurement variability with echocardiography (left) or cardiac magnetic resonance imaging. Dashed line = line of identity. Solid line = linear regression line.

Figure 5. Linear regression (top) and Bland-Altman plots (bottom) for mitral regurgitant (MR) volume measurement variability with echocardiography (left) or cardiac magnetic resonance imaging. Dashed line = line of identity. Solid line = linear regression line.

Figure 6. Linear regression (top) and Bland-Altman plots (bottom) for transaortic stroke volume measurement by Doppler LVOT flow (left) and CMR phase contrast velocity mapping (right). Dashed line = line of identity. Solid line = linear regression line.

Figure 7. Linear regression (top) and Bland-Altman plots (bottom) for stroke volume measurement based on echocardiographic c (left) and CMR (right) LV volumes. Dashed line = line of identity. Solid line = linear regression line.

Figure 8. Intermodality agreement for measurement of aortic (AR) and mitral (MR) regurgitant volume (left). The right panel shows the comparison for measurement of stroke volume by the Doppler LVOT method versus CMR phase contrast velocity mapping method and for the 2D echocardiographic versus CMR LV volume methods. Dashed line = line of identity. Solid line = linear regression line.



$$SV_{LVOT} = CSA_{LVOT} \times VTI_{LVOT}$$

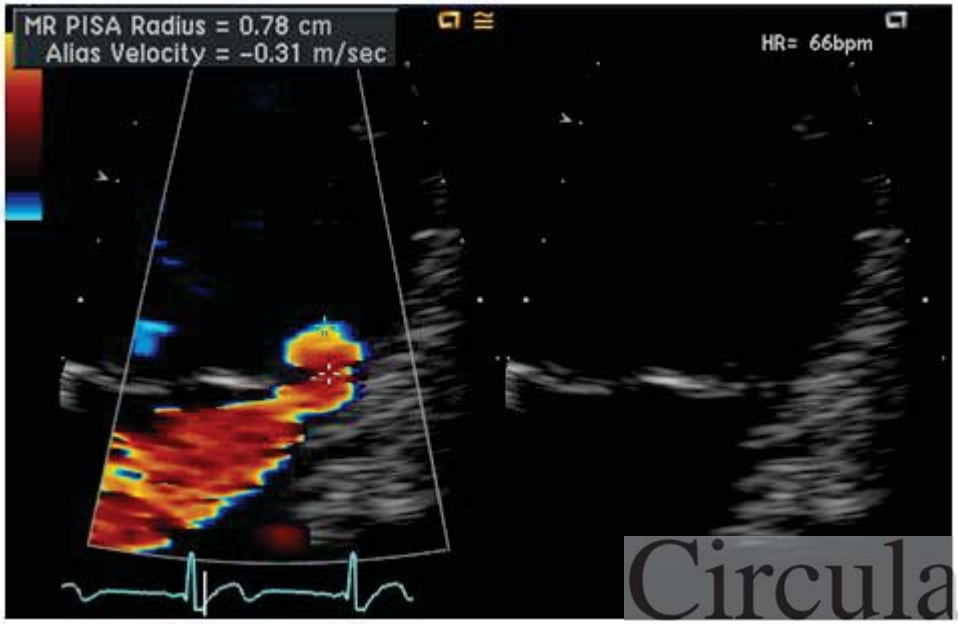
$$SV_{MA} = CSA_{MA} \times VTI_{MA}$$

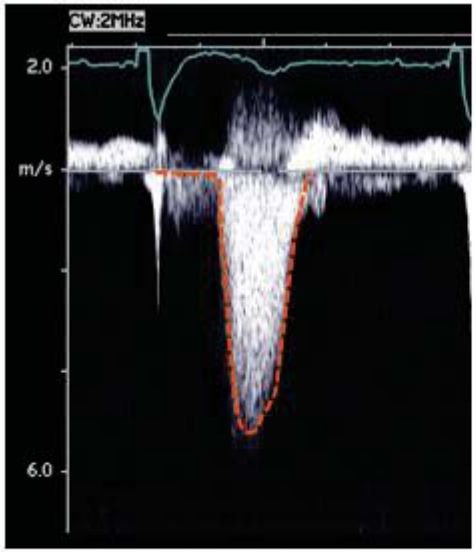
$$RVol_{AR} = [CSA_{LVOT} \times VTI_{LVOT}] - [CSA_{MA} \times VTI_{MA}]$$

$$RVol_{MR} = [CSA_{MA} \times VTI_{MA}] - [CSA_{LVOT} \times VTI_{LVOT}]$$

OR

$$RVol_{MR} = LV\text{-}SV_{2D} - [CSA_{LVOT} \times VTI_{LVOT}]$$

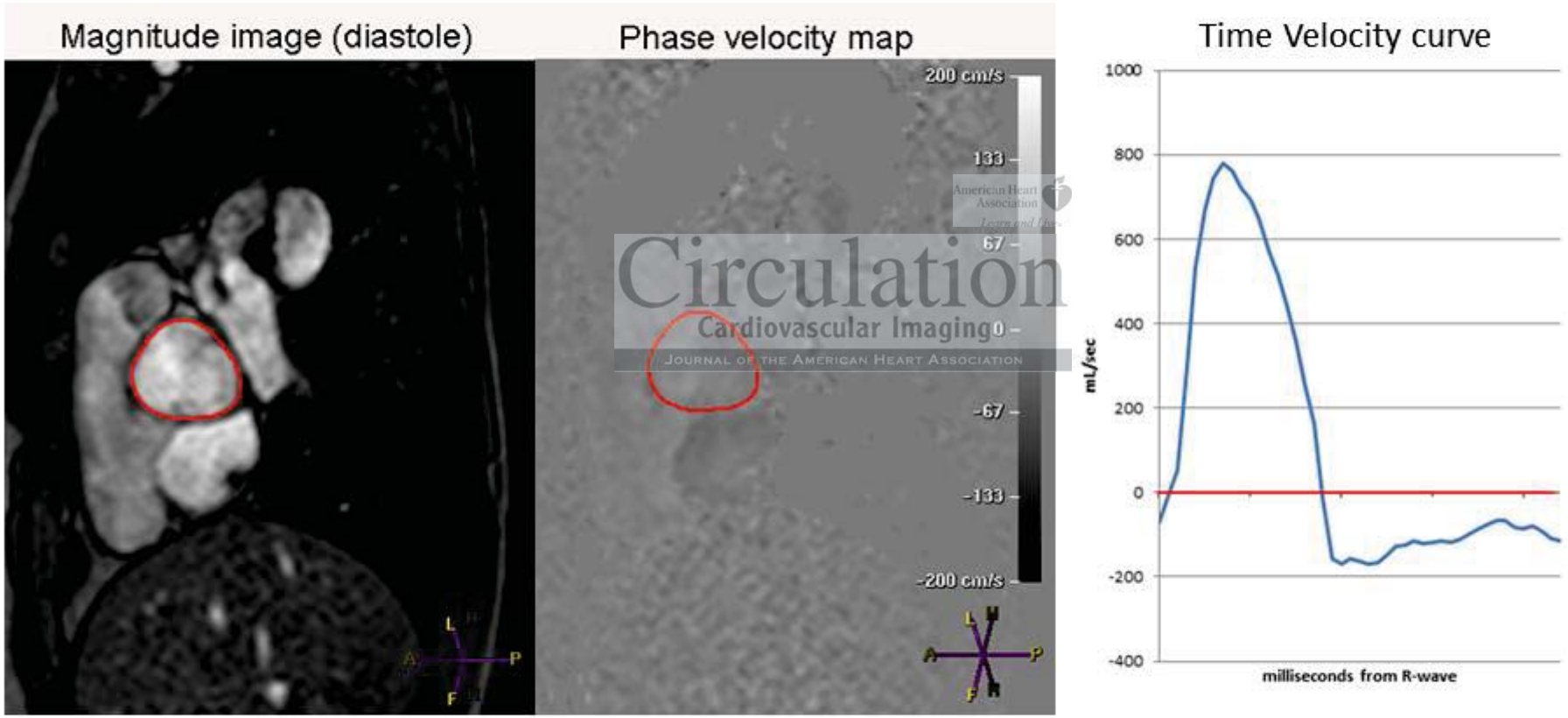


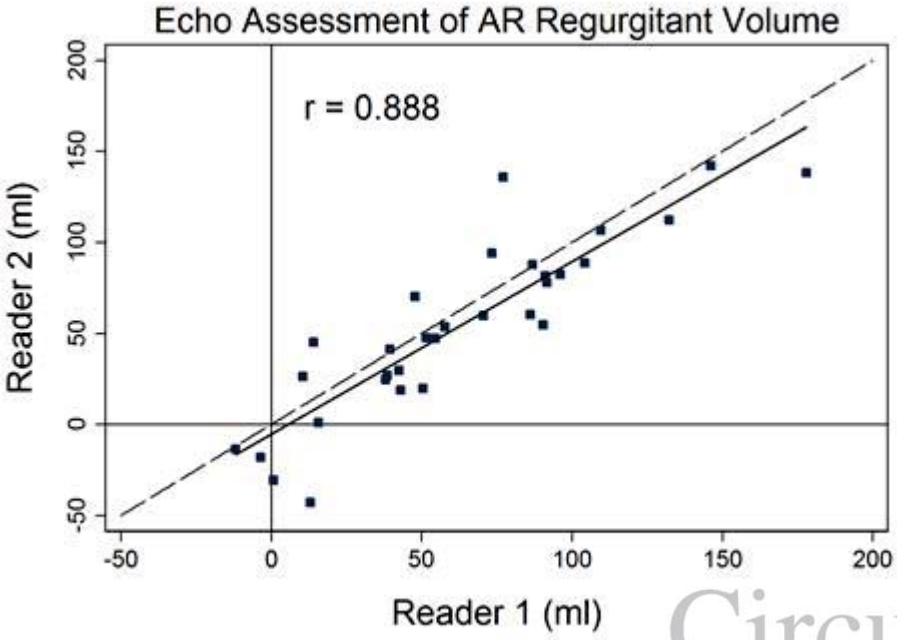


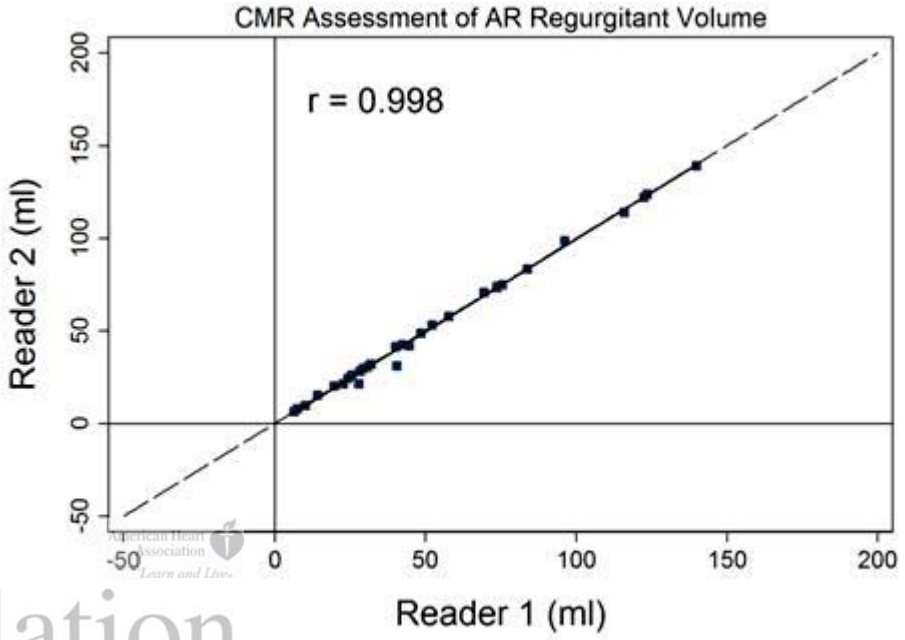
PISA flow rate
$= 2\pi r^2 \times V_{Aliasing}$

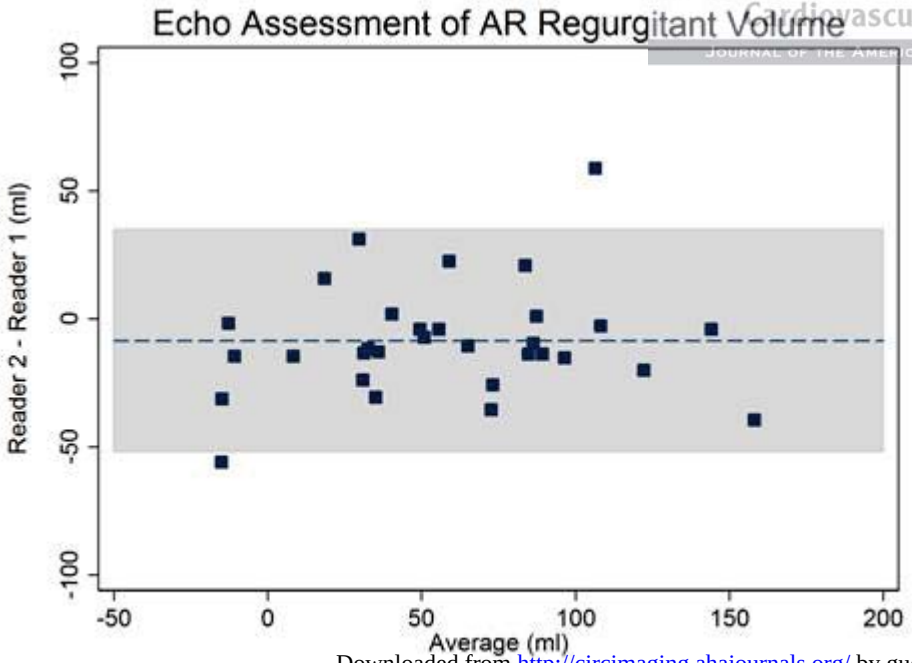
ROA
$=$ PISA flow rate $\times V_{MR}$

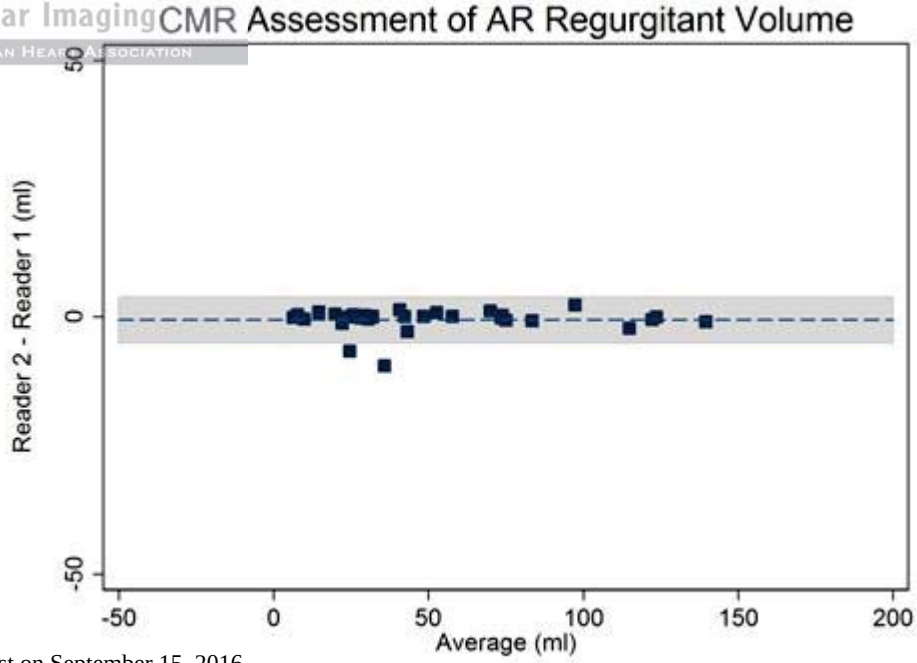
RVol
$=$ ROA $\times VTI_{MR}$

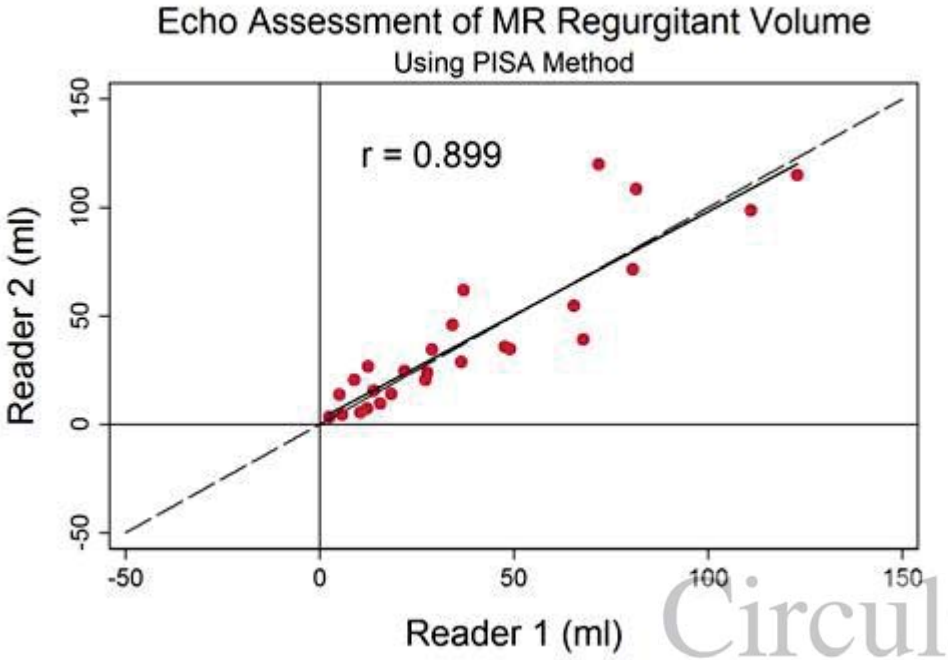


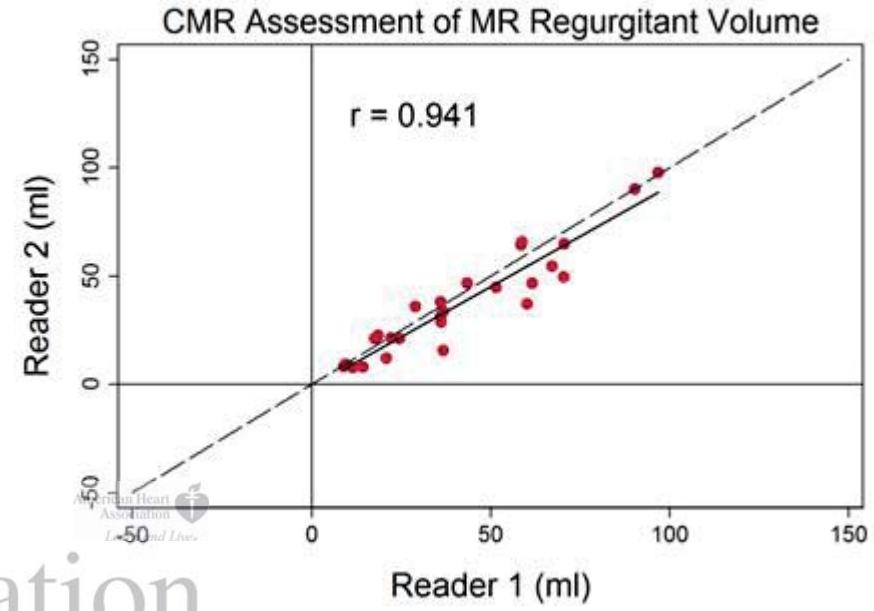


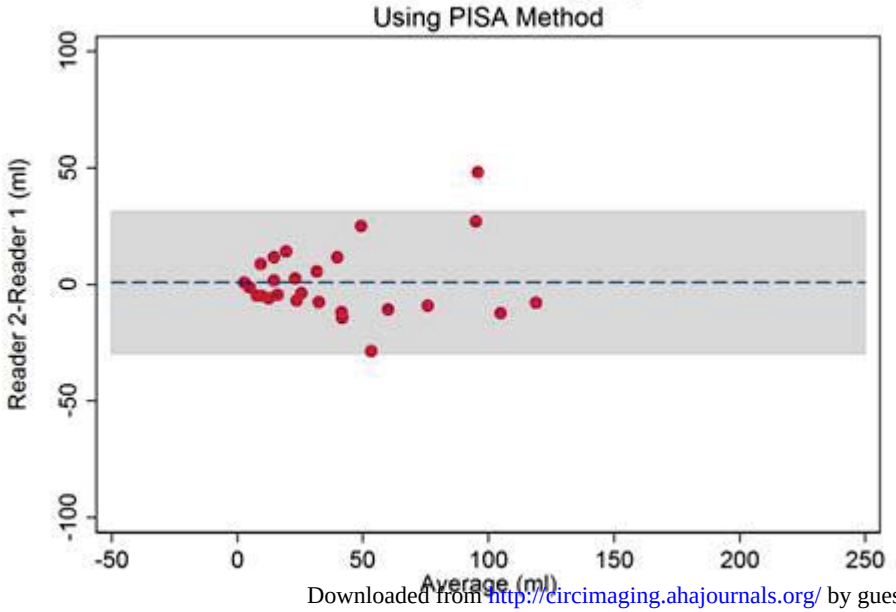


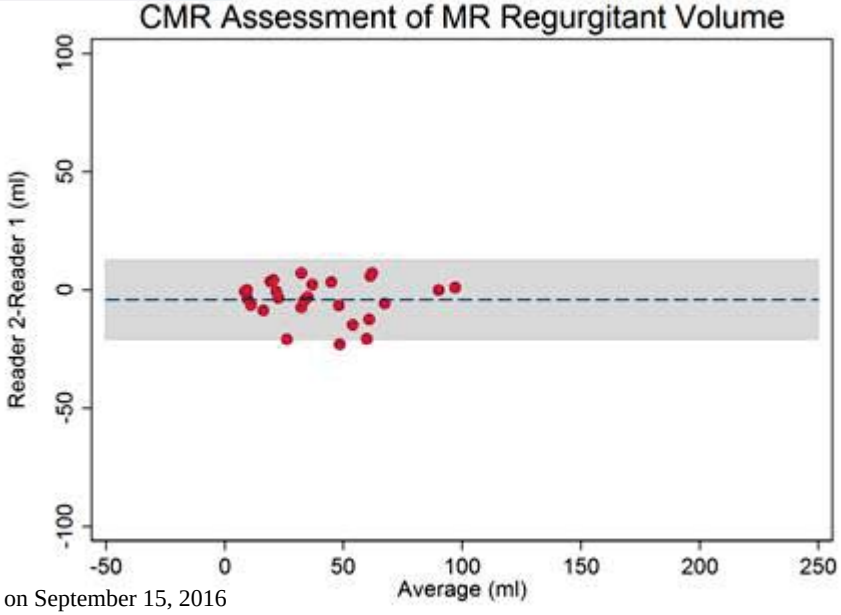


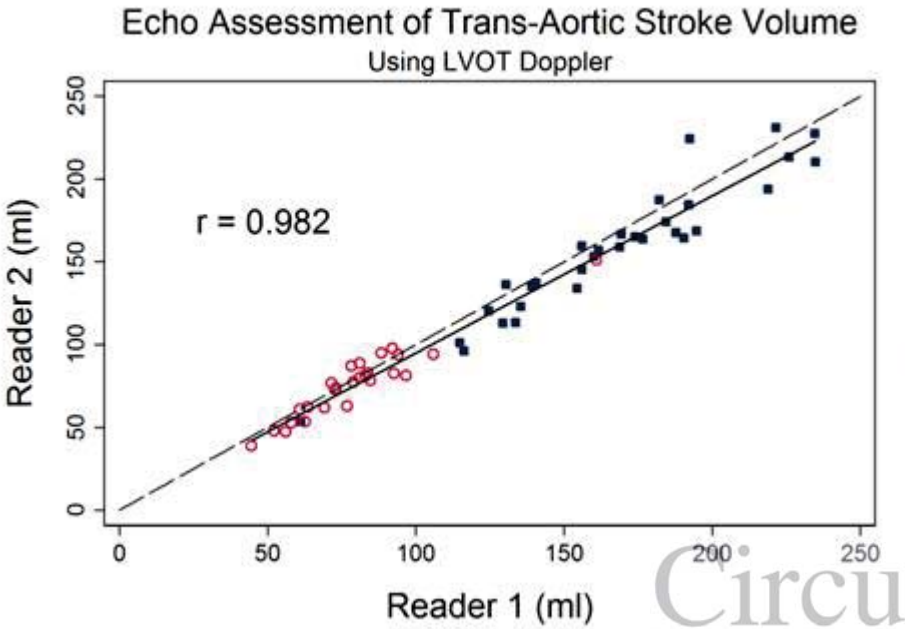


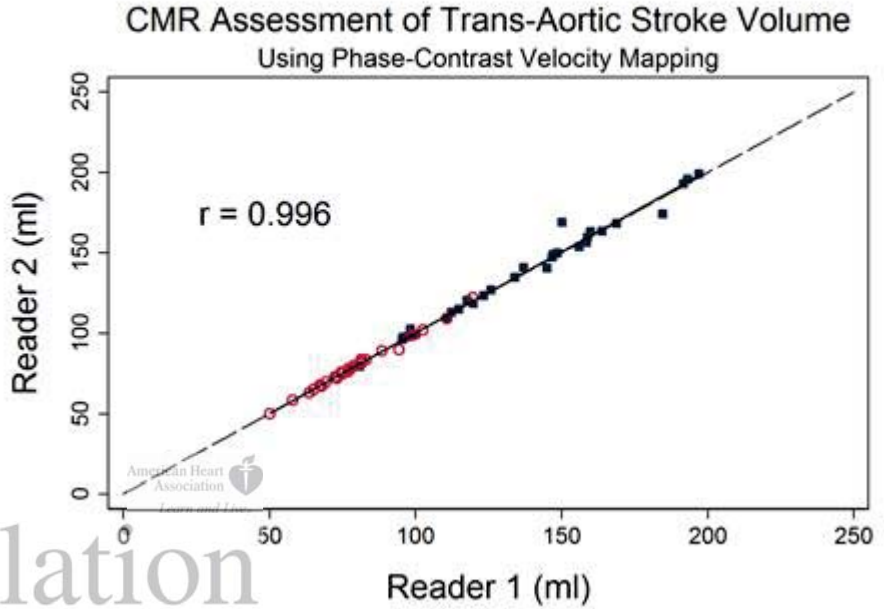


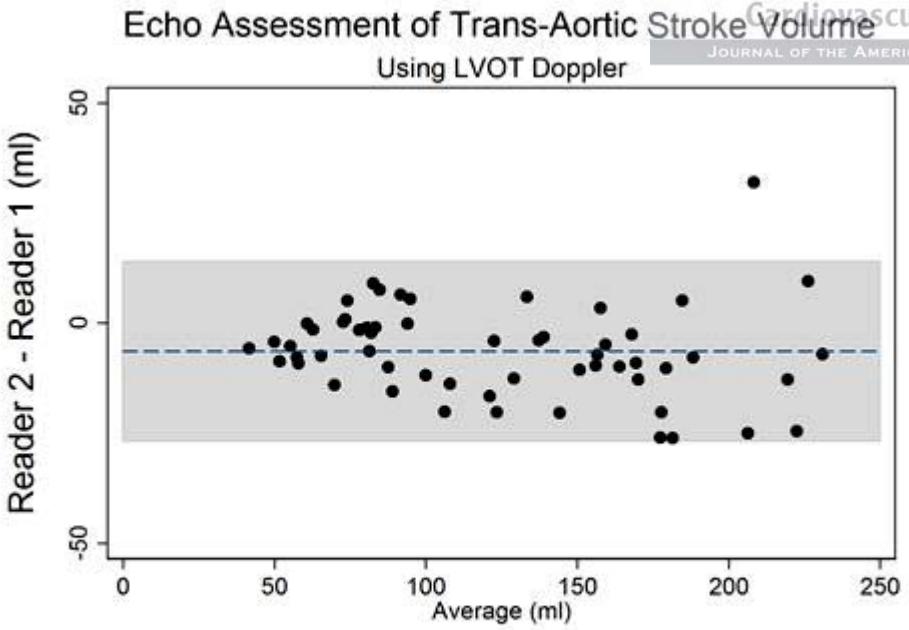


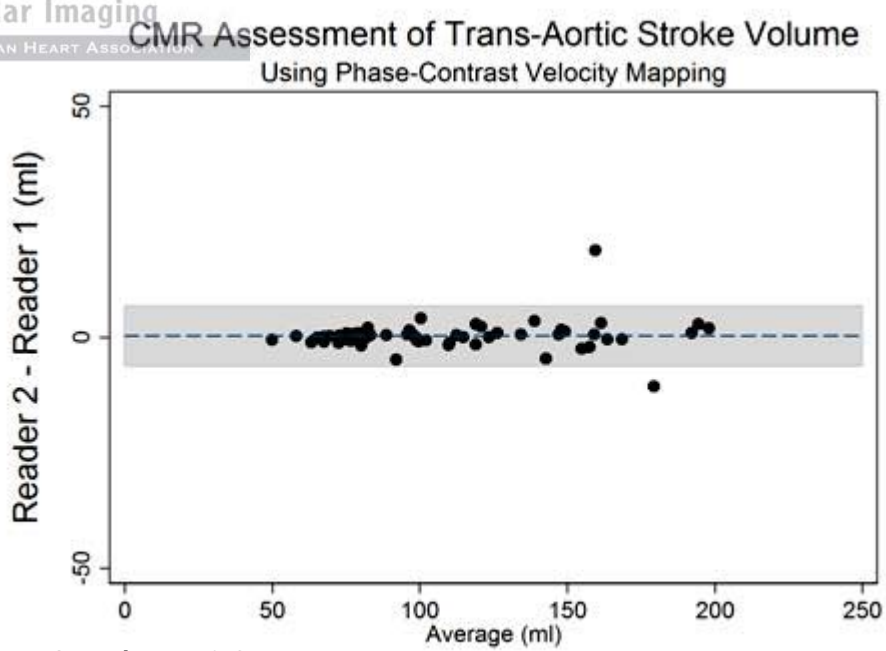


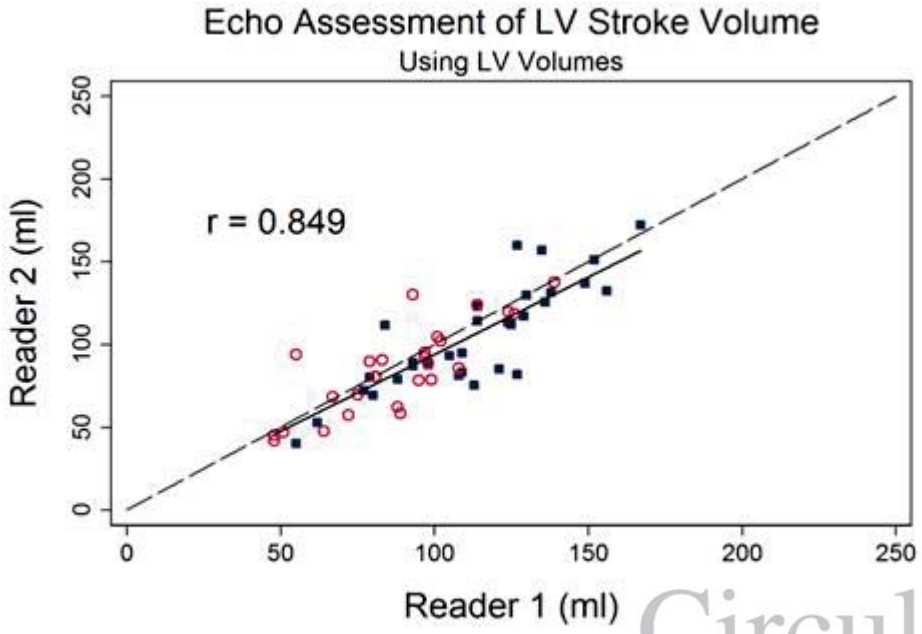


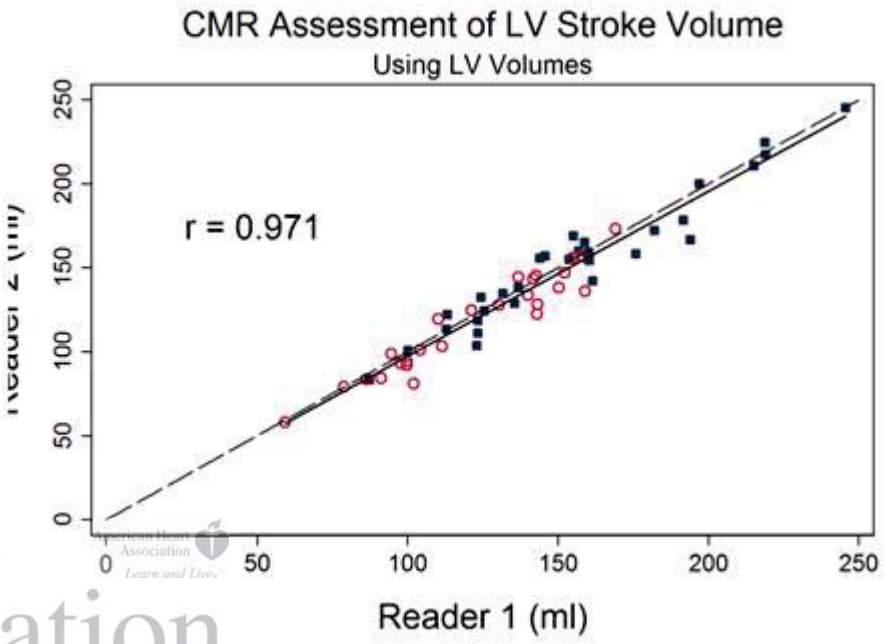


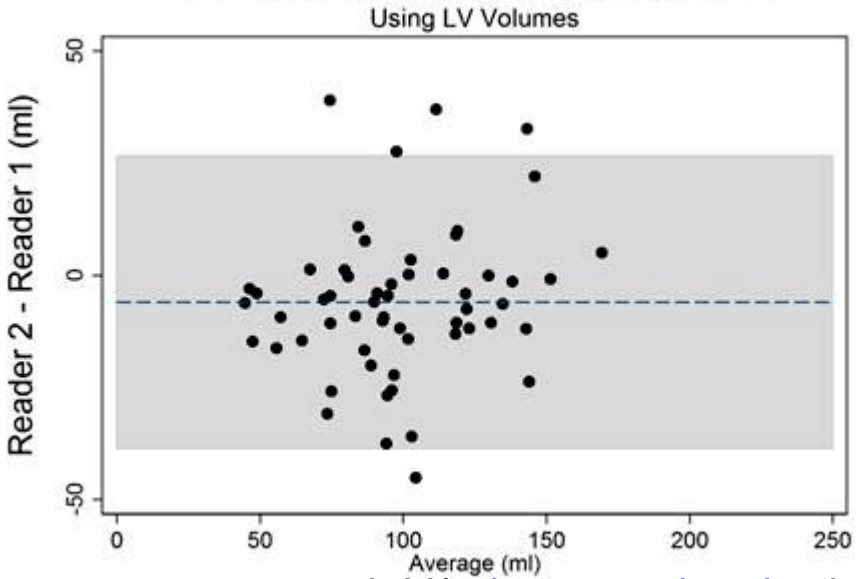


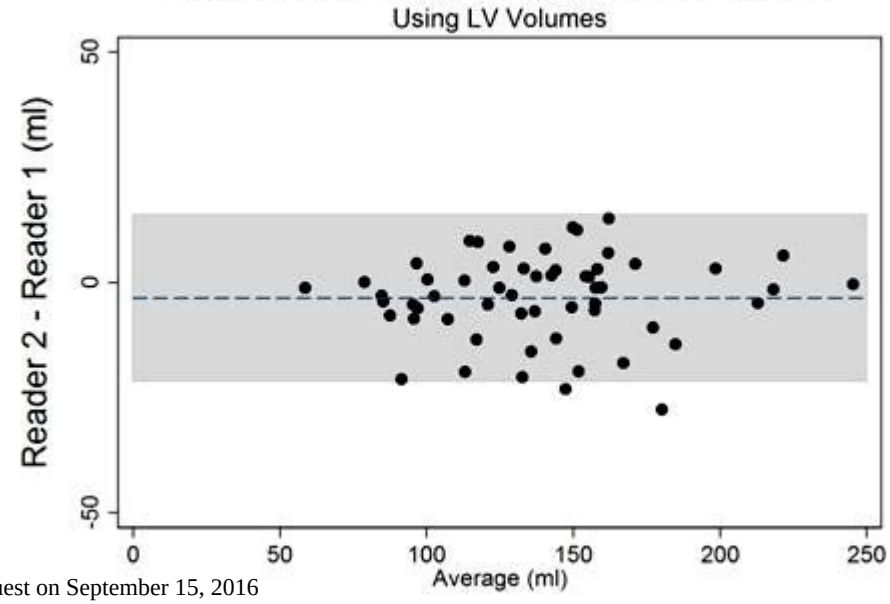


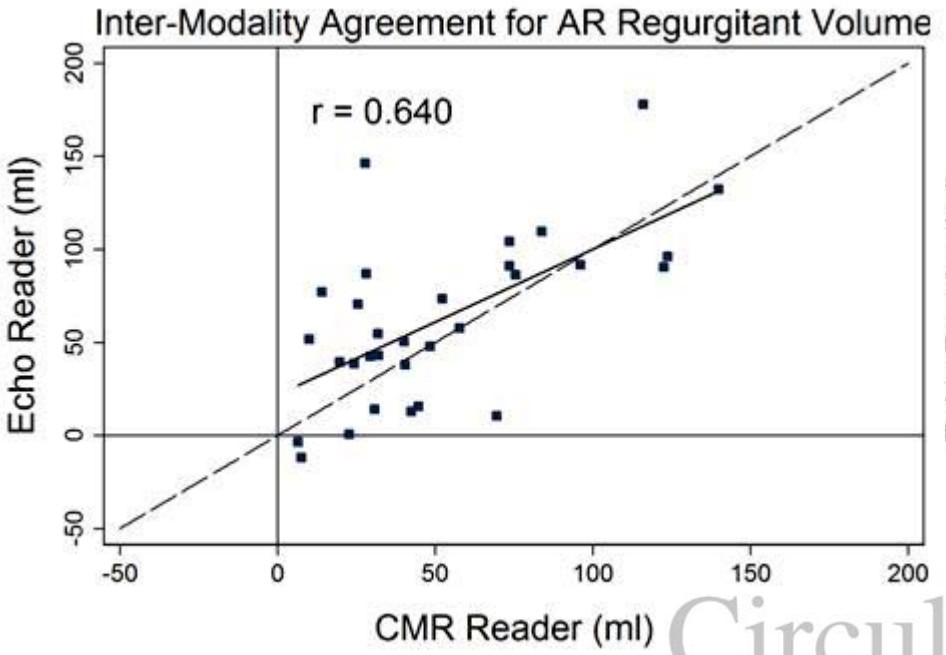


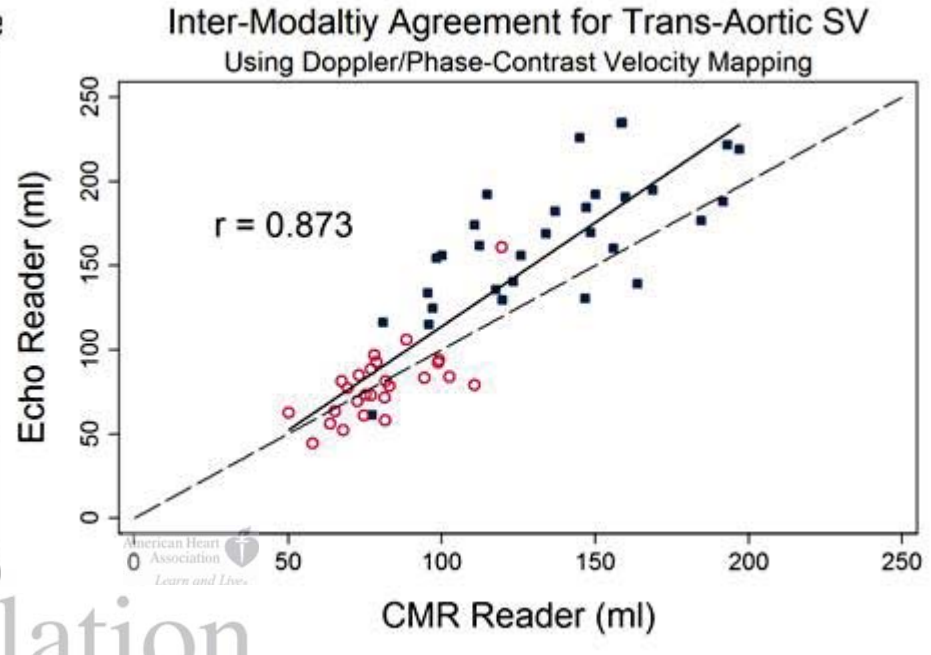


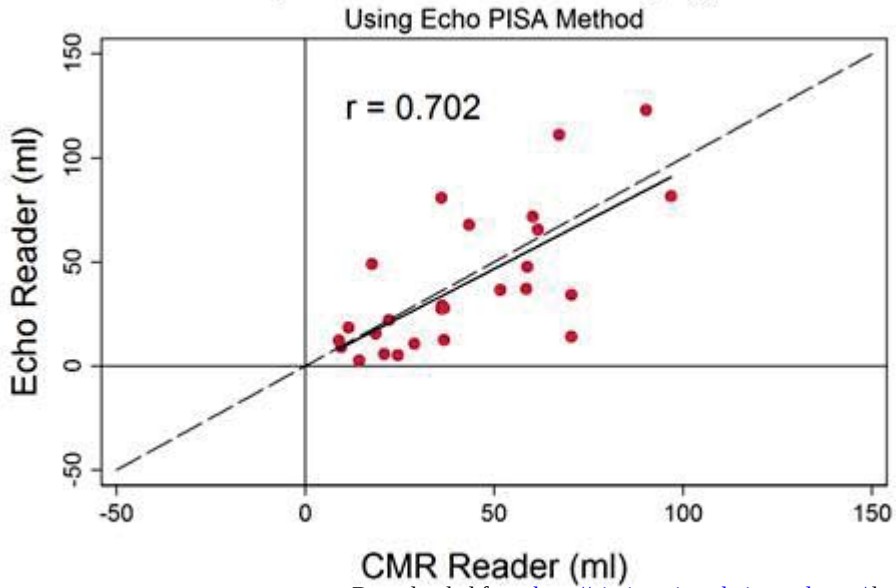


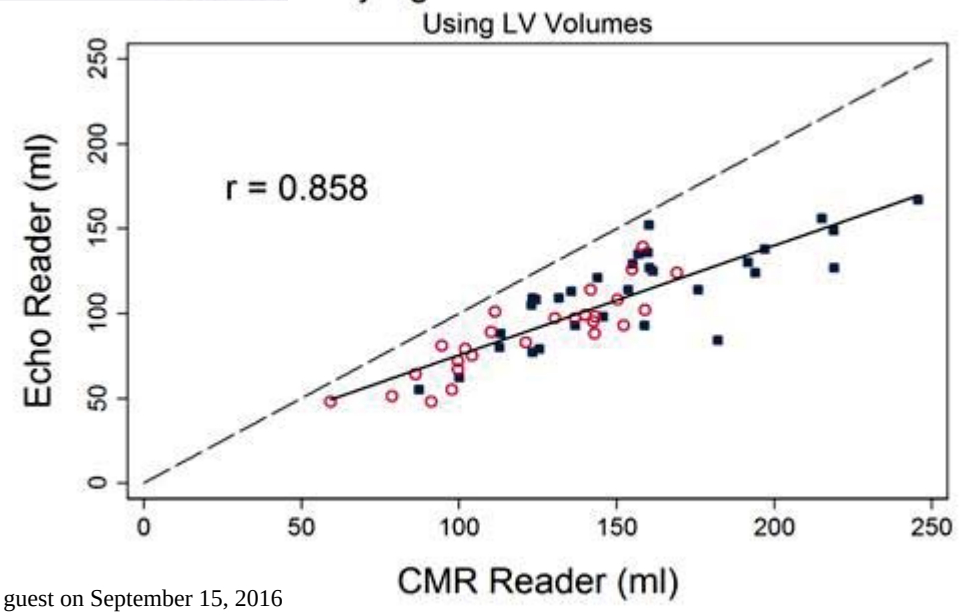












Prospective Comparison of Valve Regurgitation Quantitation by Cardiac Magnetic Resonance Imaging and Transthoracic Echocardiography

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SUPPLEMENTAL MATERIAL

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This supplemental material section has been provided by the authors to give readers additional information about their work.

Supplement to: Cawley PJ, et al. *Prospective comparison of valve regurgitation quantitation by cardiac magnetic resonance imaging and transthoracic echocardiography.*

This supplement provides additional methodology and data pertaining to statistical power calculations and to cardiac magnetic resonance (CMR) imaging quantitation of valve regurgitation based on right ventricular and left ventricular volumes.

Additional Methods

Sample size calculations

For power calculations, we estimated that the standard deviation of regurgitant volume would be approximately 10mL for each modality and that the standard deviation of regurgitant fraction would be 9% for CMR and 10% for echocardiography based on previously published data [1 2]

For inter-modality agreement, using a paired t-test with 80% power to detect a difference between means of 10mL with a $p<0.05$, the sample size needed was estimated to be n=10 patients for each group. For inter-observer and intra-observer variability, using paired t-tests to detect differences in means and two-sided $p<0.05$, we estimated the following:

	CMR		Echo	
Difference in Means	Power=0.8	Power=0.9	Power=0.8	Power=0.9
5%	N=27	N=49	N=33	N=45
10%	N=9	N=11	N=10	N=13

We recruited n=26 patients into the MR analyses, giving 80% power to detect a 5.7% difference in means at a two-sided $p<0.05$ and 90% power to detect a 6.6% difference in means. We recruited n=31 patients into the AR analyses, giving 80% power to detect a 5.2% difference in means and 90% power to detect a 6% difference in means at a two-sided $p<0.05$.

Based on these calculations, repeated measurements of n=10 AR studies and n=10 MR studies were used for intraobserver variability calculations, which yields an 80% power to detect

a mean difference of 10% at a two-sided p-value <0.05. When component measurements (e.g., LV volume) were performed in both groups, the variable was combined across groups (totaling n=20) to enhance statistical power.

Quantification of Regurgitation Using CMR Volume Method

The methodology for obtaining CMR images and performing left ventricular (LV) volume measurements are described in the accompanying manuscript. From these previously obtained images, right ventricular (RV) volumes were retrospectively measured by tracing endocardial borders on stack of short axis images. These images were obtained from breath-held steady-state free- precession (SSFP) covering the entire right ventricle, from base to apex, 1 slice/breath-hold. Papillary muscles and trabeculations were included in the blood pool on the contours. End-diastolic (EDV) and end-systolic volumes (ESV) were calculated by summation of disks, and from these volume measurements, RV stroke volume and ejection fraction were calculated.

If only a single valve has significant regurgitation, the regurgitant volume can be calculated by the difference between LV and RV stroke volumes. Aortic and mitral regurgitant volumes were thus calculated for each group by subtracting RV stroke volume from LV stroke volume as follows: Regurgitant volume (RVol) = LV stroke volume – RV stroke volume. Regurgitant fraction (RF) was further calculated as: RF = RVol /LV Stroke Volume.

The RV-LV volume method was not planned a priori and was performed retrospectively from the previously obtained CMR images. Measurements of RV volumes were performed by two investigators (EVK and WES) with SCMR Level III training in reading CMR studies. LV volumes were previously measured by two additional physicians (PJC and CHC). For AR and MR regurgitant volume and regurgitant fraction, the LV measurements performed by reader PJC

were combined with the RV measurements of reader EVK. Similarly, the LV measurements performed by reader CHC were combined with the RV measurements of reader WES. Interobserver and inter-modality variability were assessed using the methodology described in the main manuscript, using the first readings whenever repeated measures were performed. Intraobserver variability in RV volumes was performed using repeated measures by reader WES. Intraobserver variability in AR and MR regurgitant volume and fraction were performed using the measurements by readers CHC and WES.

Results

Intraobserver variability for the CMR RV-LV volume method is shown in Supplementary Table 1. For AR quantification, the intraobserver variability for this method appears higher than for CMR phase contrast velocity mapping, as assessed by Bland Altman limits of agreement, coefficient correlations and coefficient of variation. For MR quantification, the two CMR methods – which share LV volume assessment – show similar intraobserver variability.

Interobserver variability for the CMR RV-LV volume method are presented in Supplementary Table 2 and depicted in Supplementary Figures 1 & 2. Interobserver variability appears higher than for the CMR phased contrast velocity method for both aortic and mitral regurgitant volumes, with lower correlations between readers, larger limits of agreement, and higher coefficients of variation (Table 3 & Supplementary Table 2). This CMR RV-LV volume method showed similar interobserver variability compared to TTE methods (Supplementary Table 2). Interobserver variability for the RV component measurements are shown in Supplementary Table 2 & Supplementary Figure 3.

On average, the CMR RV-LV volume method of quantifying valve regurgitation provided higher estimates of regurgitant volume compared with the CMR phase contrast velocity method

for AR (68±41 vs. 52±37 ml, p<0.0001) but not for MR (41±25 vs. 42±25 ml, p=0.62). Compared to TTE methods, the CMR RV-LV volume method provided similar estimates of aortic regurgitant volume and mitral regurgitant volume assessed by PISA (Supplementary Table 3). There were significant differences in aortic regurgitant fraction and mitral regurgitant volumes assessed by the TTE Doppler at 2 sites or TTE LV volume methods. Intermodality (CMR vs. TTE) agreement for the CMR RV-LV volume method is shown in Supplementary Figure 4.

Reference List

1. Bargiggia GS, Tronconi L, Sahn DJ et al. A new method for quantitation of mitral regurgitation based on color flow Doppler imaging of flow convergence proximal to regurgitant orifice. *Circulation.* 1991;84:1481-9.

2. Hundley WG, Li HF, Willard JE et al. Magnetic resonance imaging assessment of the severity of mitral regurgitation. Comparison with invasive techniques. *Circulation.* 1995;92:1151-8.

Supplementary Table **1**: Intra-observer variability measures for CMR RV-LV Volume Method

	Bland-Altman*	r-value**	CV (%)
Aortic regurgitation (n=10)			
Regurgitant volume (mL)	-4 (-22 to 14)	0.98	15.4
Regurgitant fraction (%)	-2 (-7 to 3)	0.92	15.2
Mitral regurgitation (n=10)			
Regurgitant volume (mL)	2 (-16 to 21)	0.93	19.1
Regurgitant fraction (%)	2 (-12 to 15)	0.90	13.6
Right ventricle (n=20)			
End-diastolic volume (mL)	4 (-13 to 21)	0.97	3.8
End-systolic volume (mL)	4 (-7 to 15)	0.97	6.2
Stroke volume (mL)	0 (-18 to 18)	0.87	8.2
Ejection fraction (%)	-1 (-9 to 6)	0.84	6.3

* Mean difference (two-sided 95% confidence limits of agreement)
** Pearson Correlation (all p-values < 0.00005)
^^ $p < 0.02$ for CMR versus TTE r-value
^ $p < 0.00005$ for CMR versus TTE r-value

CV, coefficient of variation; 2D LV, left ventricular volumes measured from two dimensional echocardiography; LVOT, left ventricular outflow tact; PISA, proximal isovelocity surface area approach; ROA, regurgitant orifice area.

Supplementary Table 2: Inter-observer measurement variability for CMR RV-LV volume method.

	TTE			CMR			TTE vs CMR
	Bland-Altman*	r-value**	CV (%)	Bland-Altman*	r-value**	CV (%)	p-value^
Aortic regurgitation (n=31)							
Regurgitant volume (mL)	3 (-38 to 45)	0.92	32.1	-1.0 (-44 to 42)	0.88	30.6	NS
Regurgitant fraction (%)	3 (-24 to 30)	0.87	31.4	-0.1 (-25 to 25)	0.78	27.6	NS
Mitral regurgitation (n=26)							
Regurgitant volume (mL)				3 (-27 to 34)	0.80	45.7	
vs. TTE PISA	-4 (-29 to 22)	0.96	29.1				NS
Vs. TTE volume flow 2 sites	21 (-28 to 72)	0.85	36.5				NS
Vs. TTE 2D LV + Doppler	6 (-33 to 46)	0.93	84.5				NS
Regurgitant Fraction (%)				5 (-17 to 26)	0.76	44.9	NS
Right ventricle (n=57)							
End-diastolic volume (mL)	---	---	---	-11.9 (-43 to 20)	0.90	8.9	---
End-systolic volume (mL)	---	---	---	-7.4 (-23 to 9)	0.94	9.9	---
Stroke volume (mL)	---	---	---	-4.3 (-31 to 22)	0.76	12.0	---
Ejection fraction (%)	---	---	---	0.7 (-8 to 10)	0.77	6.5	---

* Mean difference (two sided 95% confidence limits of agreement)
** Pearson Correlation (all p-values < 0.00005)
^p-value comparing TTE and CMR correlations
Abbreviations as in Supplementary Table 1.

Supplementary Table 3: CMR versus Echo Measurements

	TTE	CMR	TTE vs. CMR	
	Mean ± SD	Mean ±SD	t-test	r-value*
Aortic regurgitation (n=31)				
Regurgitant volume (mL)	62 ± 45	68 ± 42	0.36	0.66
Regurgitant fraction (%)	34 ± 21	41 ± 17	0.04	0.55
Mitral regurgitation (n=26)				
Regurgitant volume (mL)		41 ± 25		
PISA	39 ± 33		0.71	0.69
Volume flow 2 sites	79 ± 61		0.0006	0.65
2D LV + Doppler	9 ±31		<0.0001	0.57
Regurgitant Fraction	44 ± 24	31 ± 16	0.003	0.74
Right ventricle (n=57)				
End-diastolic volume (mL)	---	167 ± 35	---	---
End-systolic volume (mL)	---	83 ± 24	---	---
Stroke volume (mL)	---	85 ± 18	---	---
Ejection fraction (%)	---	51 ± 7	---	---

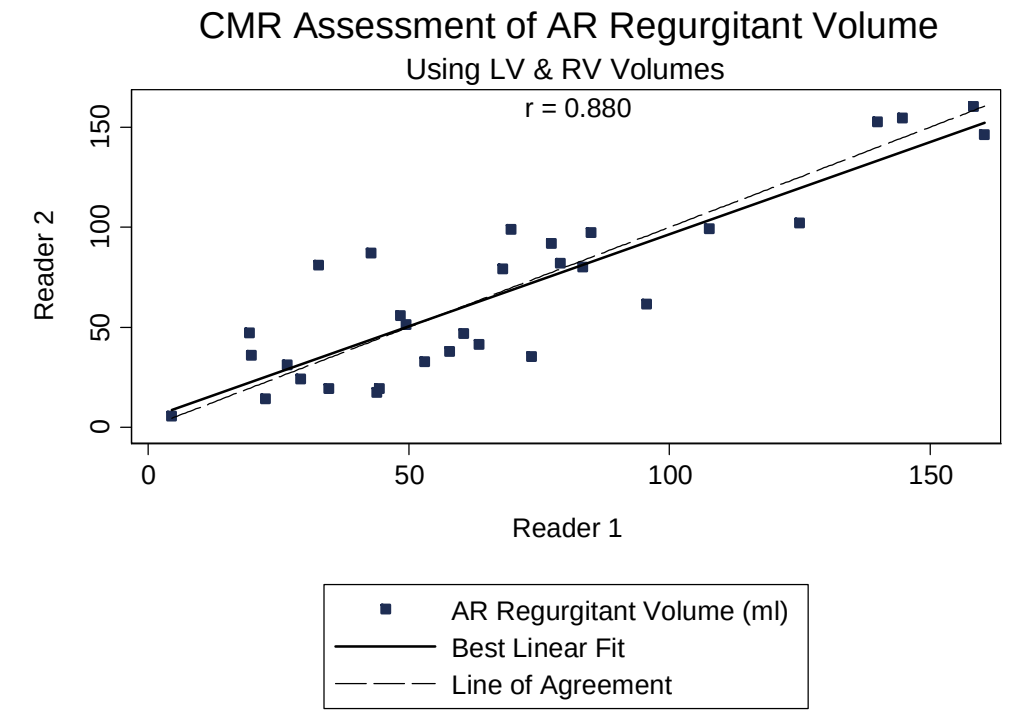
Supplementary Figure 1: Linear regression (top) and Bland-Altman plots (bottom) for aortic regurgitant (AR) volume measurement variability by cardiac magnetic resonance (CMR) imaging. Dashed line = line of identity. Solid line = linear regression line.

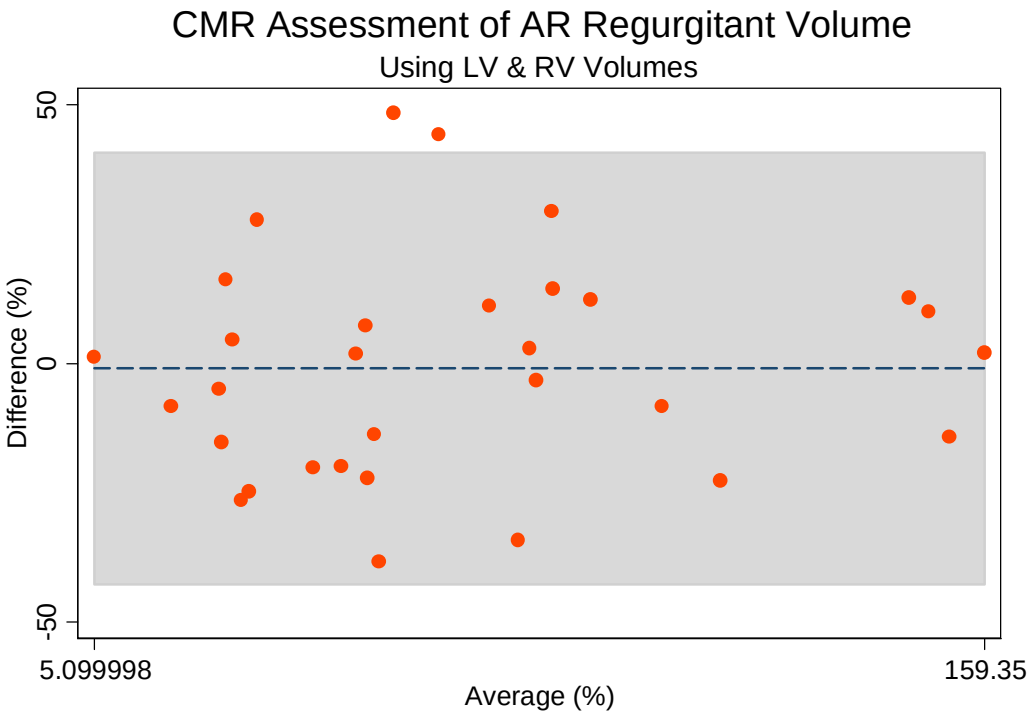
Supplementary Figure 2: Linear regression (top) and Bland-Altman plots (bottom) for mitral regurgitant (MR) volume measurement variability by cardiac magnetic resonance (CMR) imaging. Dashed line = line of identity. Solid line = linear regression line.

Supplementary Figure 3: Linear regression plots for right ventricle end diastolic volume (top left), right ventricular end systolic volume (top right), right ventricle stroke volume (bottom left) and right ventricular ejection fraction (bottom right). Dashed line = line of identity. Solid line = linear regression line. Blue = AR subject, red = MR subject.

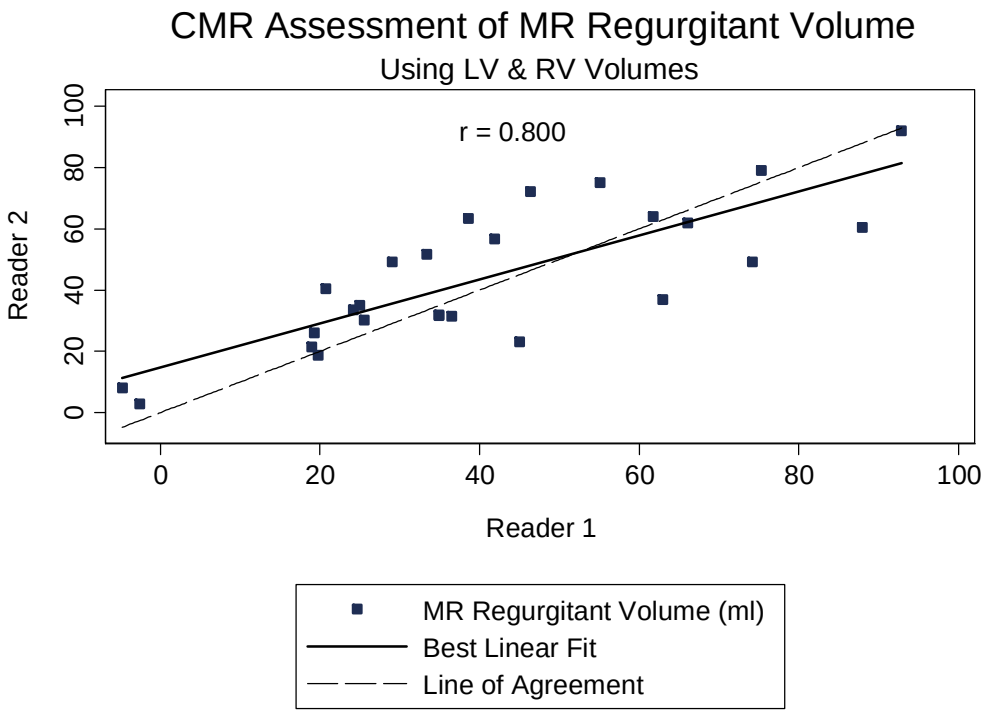
Supplementary Figure 4: Intermodality agreement for measurement of TTE vs. CMR aortic regurgitant (AR) volumes (top) and mitral regurgitant (MR) volumes (bottom). The PISA method is depicted for TTE MR quantitation. Dashed line = line of identity. Solid line = linear regression line.

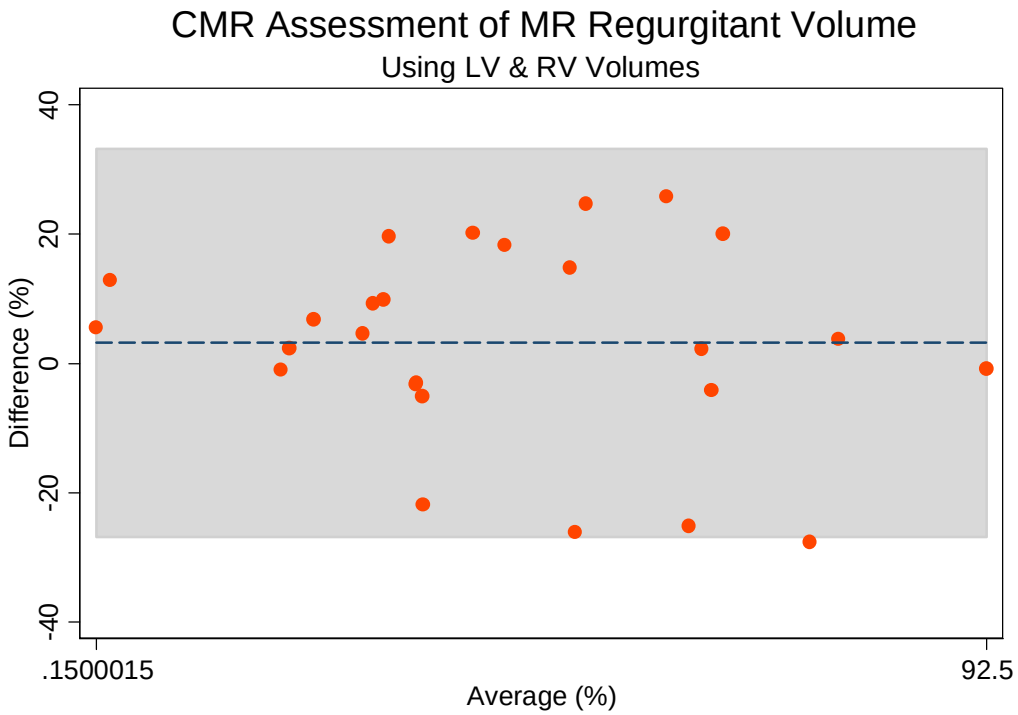
Supplementary Figure 1



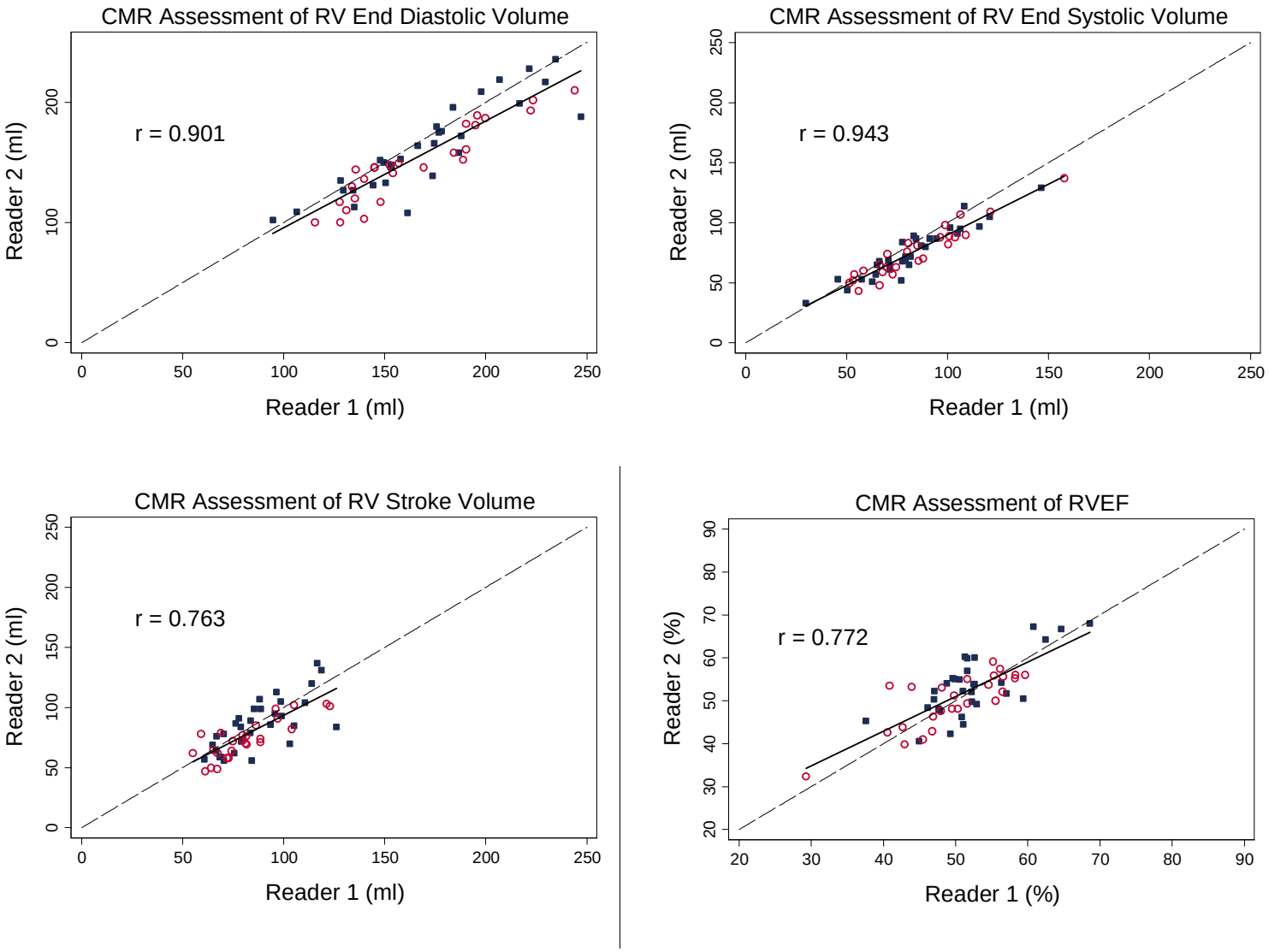


Supplementary Figure 2





Supplementary Figure 3



Supplementary Figure 4: