

## VALVULAR HEART DISEASE

# A hybrid approach for quantification of aortic valve stenosis using cardiac magnetic resonance imaging and echocardiography

DARIUSCH HAGHI, M.D.,<sup>1,\*</sup> THEANO PAPAVALASSILIU, M.D.,<sup>1</sup> GABOR KALMAR, M.D.,<sup>1</sup> MEIKE SCHRODER, M.D.,<sup>2</sup> WOLFGANG NEFF, M.D.,<sup>2</sup> JENS J. KADEN, M.D.,<sup>1</sup> UTE MULLER,<sup>1</sup> KARL K. HAASE, M.D., F.A.C.C.,<sup>1</sup> MARTIN BORGGREFE, M.D.,<sup>1</sup> and TIM SUSELBECK, M.D.<sup>1</sup>

<sup>1</sup>*Medical Department, University Hospital Mannheim, Mannheim, Germany*

<sup>2</sup>*Department of Radiology, University Hospital Mannheim, Mannheim, Germany*

**Background.** Doppler-derived calculation of aortic valve area (AVA) using the continuity equation can be difficult at times, e.g. due to poor acoustic windows, heavy calcification of the aortic valve, or significant flow acceleration in the left ventricular outflow tract. The aim of this study was to compare AVA as assessed by means of transthoracic echocardiography (TTE) with a hybrid approach, where the Doppler-derived numerator in the continuity equation was replaced by cardiovascular magnetic resonance (CMR) determination of stroke volume. **Methods.** Twenty consecutive patients admitted for evaluation of aortic stenosis underwent transthoracic echocardiography and CMR determination of stroke volume within a time period of 3 weeks. Additionally, continuous-wave Doppler spectra of the aortic valve were acquired immediately after the CMR examination. **Results.** There was no statistically significant difference for mean AVA between the two methods ( $0.88 \pm 0.23 \text{ cm}^2$  by the standard continuity equation versus  $0.86 \pm 0.23 \text{ cm}^2$  by the hybrid approach,  $p = 0.55$ ;  $r = 0.73$ ,  $p < 0.01$ ). The mean difference was  $0.02 \text{ cm}^2$  and the limits of agreement were  $-0.32$  to  $0.36$ . Only 2 patients were classified differently by the two methods. Intraobserver and interobserver variability and reproducibility were superior for the hybrid approach. **Conclusion.** The hybrid method for determination of AVA is an excellent alternative to the standard approach by TTE.

**Key Words:** Aortic stenosis; Echocardiography; Cardiovascular magnetic resonance imaging; Hybrid approach

## 1. Introduction

Evaluation of aortic valve stenosis by means of Doppler echocardiography has gained widespread acceptance in clinical routine and results have been shown to correlate well with invasive measurements (1–5). Doppler-derived calculation of aortic valve area (AVA) using the continuity equation (CE) requires measurement of the left ventricular outflow tract (LVOT) diameter, the integral of pulsed wave Doppler velocity in the LVOT and the integral of continuous wave Doppler velocity through the stenotic valve. However, accurate measurement of one or more of these parameters is not always possible. Reasons include poor acoustic windows,

heavy calcification of the aortic valve, and flow acceleration in the LVOT. When these circumstances occur, alternative methods must be used to independently validate calculated AVAs. These methods include replacing the Doppler-derived stroke volume (SV) in the CE by Simpson's biplane method of disks (6), echocardiographic planimetry of the aortic valve (7, 8), use of transpulmonary contrast agents for better image quality (9), and invasive calculation by applying the Gorlin formula. Recently, cardiac magnetic resonance (CMR) has also been used to assess AVA either by planimetry (10–12) or by velocity-encoded CMR (13). However, none of these methods is superior overall and all have inherent shortcomings. Thus, there is still a need for an alternative to the standard CE in selected patients.

Because CMR is an ideal technique for evaluation of cardiac volumes, we sought to compare AVA measurements by the standard CE with a hybrid approach, where the numerator of the CE (stroke volume) was determined by CMR and the denominator (velocity-time integral of continuous wave Doppler through the stenotic valve) was determined by echocardiography.

Received 25 August 2004; accepted 5 January 2004.

\*Address correspondence to Dr. Dariusch Haghi, M.D., I. Medizinische Klinik, Universitätsklinikum Mannheim, Mannheim 68167, Germany; Fax: 0049-621-3834082; E-mail: dariush.haghi@med.ma.uni-heidelberg.de

## 2. Methods

### 2.1. Patients

The study population consisted of 20 consecutive patients referred for evaluation of aortic stenosis. Exclusion criteria included presence of left-to-right shunting, presence of more than 2+ mitral regurgitation, presence of tachyarrhythmias (rate-controlled atrial fibrillation was not an exclusion criteria), and general exclusion criteria for CMR (14). The protocol was approved by the local institutional review board. Informed consent was obtained in all patients.

### 2.2. Study design

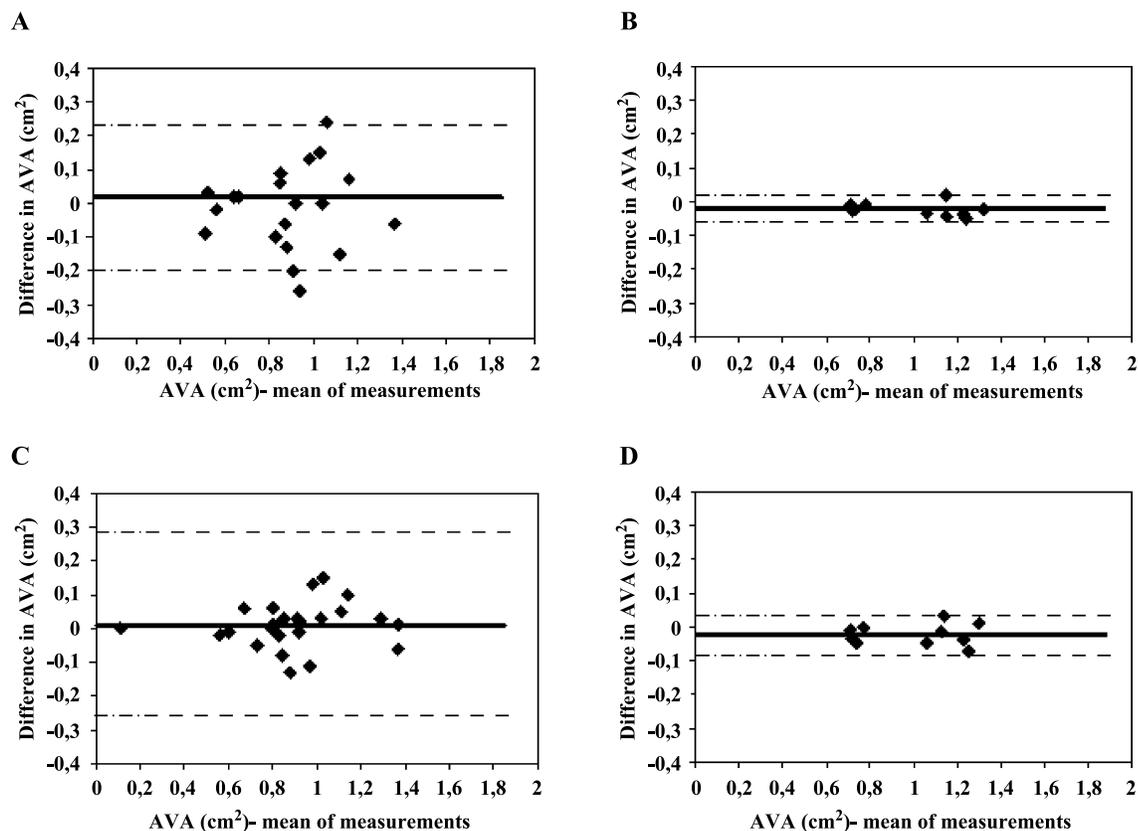
CMR and a complete echocardiographic examination were performed within a time period of 3 weeks. Immediately after the CMR examination, all patients were brought to the cardiac ultrasound laboratory for acquisition of continuous-wave Doppler spectra of the aortic valve. Heart rate was registered both during CMR and the Doppler examination to ensure that data acquisition was performed approximately at

the same heart rate. Ejection fraction was calculated from CMR data.

### 2.3. Echocardiography

All studies were performed and analyzed by the same experienced physician sonographers (DH and GK) on a commercially available system (Vivid FiVe, GE VingMed Ultrasound, Horton, Norway). Images were digitally recorded and analyzed offline using commercial software (Echopac 6.3, GE-Vingmed, Horton, Norway).

The LVOT diameter (LVOTd) was measured in the parasternal long-axis view. Doppler flow data from the LVOT were acquired in the pulsed wave mode from the apical 5-chamber view. Peak velocity across the aortic valve was measured in the same view with continuous-wave Doppler and also from apical, right parasternal, and suprasternal windows. A total of 3 measurements were performed for each parameter for patients in sinus rhythm, and 5 were performed for patients in atrial fibrillation. AVA was calculated according to the continuity equation  $AVA = (\pi \times [0.5 \times LVOTd]^2 \times LVOT \text{ velocity time integral}) / \text{transaortic}$



**Figure 1.** Intraobserver (A) and interobserver (C) variability of AVA measured by standard continuity equation. Intraobserver (B) and interobserver (D) variability of AVA measured by cardiovascular magnetic resonance. The continuous line represents the mean difference, and the dashed lines represent limits of agreement.

**Table 1.** Variability and reproducibility of echocardiographic and CMR parameters

Parameter	Mean (SD) of differences	Limits of agreement	Coefficient of repeatability
Transaortic VTI (intraobserver)	0.01 (0.05)	−0.09 to 0.11	0.10
Transaortic VTI (interobserver)	0.01 (0.05)	−0.09 to 0.10	0.10
AVA by standard CE (intraobserver)	0.02 (0.11)	−0.2 to 0.23	0.24
AVA by standard CE (interobserver)	0.01 (0.14)	−0.26 to 0.28	0.28
AVA by hybrid approach (intraobserver)	−0.02 (0.02)	−0.06 to 0.02	0.06
AVA by hybrid approach (interobserver)	−0.02 (0.03)	−0.08 to 0.04	0.07

AVA, aortic valve area; CE, continuity equation; SD, standard deviation; VTI, velocity-time integral.

velocity time integral. Severity of aortic stenosis was defined as follows: severe stenosis,  $AVA < 1.0 \text{ cm}^2$ ; moderate stenosis,  $AVA 1.0 \text{ to } 1.5 \text{ cm}^2$ ; and mild stenosis,  $AVA > 1.5 \text{ cm}^2$ .

#### 2.4. CMR

All studies were performed on a 1.5 Tesla whole body imaging system (Magnetom Sonata, Siemens Medical Systems, Erlangen, Germany). A dedicated four-element, phased-array cardiac coil was used. Images were acquired during repeated end-expiratory breath-holds. Scout images were obtained for planning of the final double-oblique long-axis and short-axis views. ECG-gated cine images were then acquired using a segmented steady state free precession sequence (True-FISP); TE/TR 1.2/3.2ms, temporal resolution 35 ms,  $1.4 \times 1.8 \times 5 \text{ mm}^3$ ). Three long-axis views and 7 to 12 short-axis views 1 cm apart covering the whole left ventricle were obtained. Scanning time for the short-axis slices ranged between 10–15 minutes. Analysis was performed using the ARGUS software package (Siemens Medical Systems, Erlangen, Germany). The cine loops were reviewed, and the end-diastolic and end-systolic frames were identified for each short-axis slice position. End-diastole was defined as the frame showing the largest cavity area, and end-systole was defined as the frame revealing the smallest cavity area. Epicardial and endocardial contours were outlined manually on each short-axis frame. For volume determination, the areas subtended by the endocardial tracings were determined in each end-diastolic and end-systolic slice and multiplied by slice thickness to yield the end-diastolic and end-systolic volumes. Total end-diastolic and end-systolic cavity volumes were obtained after the summation of data of all individual slices. Stroke volume was calculated as the

difference between end-diastolic and end-systolic volumes, and the ejection fraction (EF) was calculated as the stroke volume divided by the end-diastolic volume multiplied by 100. Analysis time averaged 20 min per subject.

#### 2.5. Hybrid technique

The numerator (stroke volume) of the CE was determined by CMR and the denominator (velocity-time integral of continuous wave Doppler through the stenotic valve) was determined by echocardiography. AVA was calculated according to the CE:  $AVA = \text{Stroke volume (by CMR)} / \text{trans-aortic velocity time integral (by echocardiography)}$ .

#### 2.6. Statistical analysis

Data are expressed as mean  $\pm$  SD. Comparisons of the results of the different methods for the same individuals were performed by standard paired student *t*-test and by the method described by Bland and Altman (15).  $P < 0.05$  was considered significant for all comparisons. Simple linear correlation with Pearson coefficient was also used. Variability of echocardiographic measurements was assessed on all studies and variability of CMR measurements was assessed on 10 randomly selected studies. Intraobserver variability was calculated as the standard deviation of the differences between the first and second determination for a single observer, expressed as a percent of the average value. Interobserver variability was calculated as the standard deviation of the differences between the two observers, expressed as the percent of the average value. Repeatability coefficient (RC) was defined as 2 standard deviations of differences between the first and second

**Table 2.** Comparison between standard continuity equation and hybrid approach

Number of patients	AVA by standard CE (Mean $\pm$ SD)	AVA by hybrid approach (Mean $\pm$ SD)	Mean difference ( $\text{cm}^2$ )	Limits of agreement ( $\text{cm}^2$ )	P value
20	$0.88 \pm 0.23 \text{ cm}^2$	$0.86 \pm 0.23 \text{ cm}^2$	0.02	−0.33 to 0.36	0.55

AVA, aortic valve area; CE, continuity equation; SD, standard deviation.

determination for a single observer (intraobserver RC) or between the two observers (interobserver RC).

### 3. Results

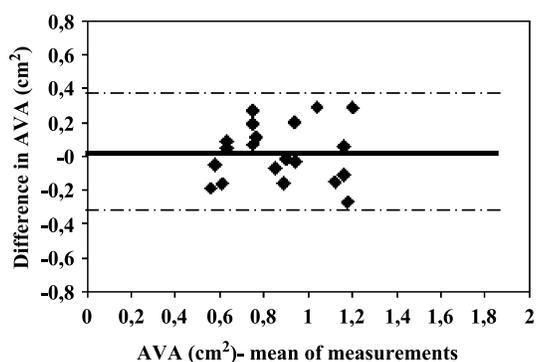
CMR could not be performed in one patient because of severe claustrophobia and, in another patient, due to an implanted pacemaker. In all, 20 patients (13 men, 7 women), ranging from 40–84 years (mean 72) were included in the study. Two patients were in rate-controlled atrial fibrillation, and 18 patients were in sinus rhythm. All patients had either moderate or severe aortic stenosis and none of the patients had severe aortic regurgitation. Ejection fraction ranged from 25% to 80% (mean 59%). One patient had low gradient aortic stenosis.

#### 3.1. Echocardiography

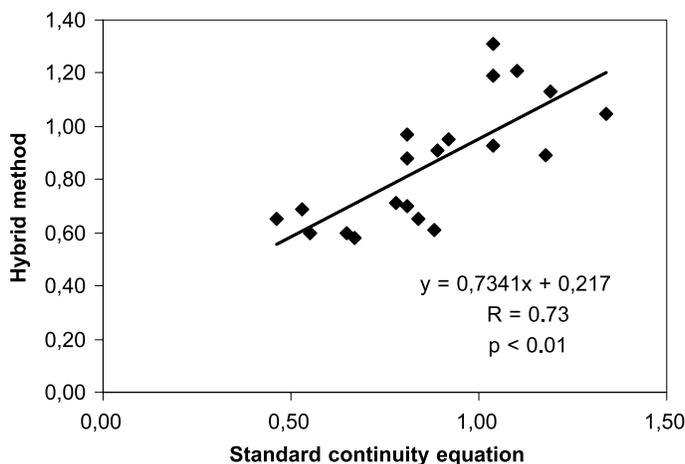
AVA ranged 0.46 to 1.34 cm<sup>2</sup> (mean 0.88 ± 0.23 cm<sup>2</sup>). Aortic valve stenosis was severe in 13 patients and moderate in 7. Intraobserver and interobserver coefficient of variation were both 5% for the velocity-time integral (VTI) across the aortic valve and 13% and 16% for AVA, respectively. Intraobserver and interobserver RC were both 10% for VTI and 24% and 27% for AVA, respectively. Bland-Altman analysis is shown in Fig. 1. Results are summarized in Table 1.

#### 3.2. CMR

AVA ranged 0.47 to 1.31 cm<sup>2</sup> (mean 0.86 ± 0.23 cm<sup>2</sup>). Aortic valve stenosis was severe in 15 patients and moderate in 5. Intraobserver and interobserver coefficient of variation were 2% and 3% for AVA, respectively. Intraobserver and interobserver RC were 6% and 7%, respectively. Bland-Altman analysis is shown in Fig. 1. Results are summarized in Table 1.



**Figure 2.** Agreement between AVA measured by standard continuity equation and hybrid approach. The continuous line represents the mean difference, and the dashed lines represent limits of agreement.



**Figure 3.** Linear regression graph of correlation between standard continuity equation and hybrid method.

#### 3.3. Comparing the hybrid approach with standard continuity equation

Results for calculation of AVA are summarized in Table 2 and Bland-Altman plots are shown in Fig. 2. There was no statistically significant difference for mean AVA between the two methods (0.88 ± 0.23 cm<sup>2</sup> versus 0.86 ± 0.23 cm<sup>2</sup>, p = 0.55). Correlation between both methods was good (r = 0.73, p < 0.01) (Fig. 3). Mean difference (bias) was 0.02 cm<sup>2</sup>, and the limits of agreement were −0.32 to 0.36. Only 2 patients were classified differently by the two methods. Both had severe aortic valve stenosis by the hybrid approach (0.89 cm<sup>2</sup> and 0.93 cm<sup>2</sup>, respectively) and moderate stenosis by the standard CE (1.18 cm<sup>2</sup> and 1.04 cm<sup>2</sup>, respectively).

### 4. Discussion

Calculation of AVA by means of Doppler echocardiography has become the accepted standard for evaluation of aortic valve stenosis in everyday clinical practice, as it is non-invasive, readily available, and can be performed at reasonable cost. This method has been validated in numerous studies in the past (1–5). Calculation of AVA by applying the continuity equation requires measurement of the LVOTd and the LVOT flow velocity. Accurate measurement of LVOTd can be affected by severe calcification of the aortic valve or by poor echogenicity of the patient (6, 16) and flow acceleration in the LVOT can lead to overestimation of the numerator of the continuity equation, thereby overestimating the true AVA (6, 17). To elude these limitations, a modified continuity equation has been proposed by Dumont et al. (6) where the numerator of the equation has been replaced by the difference between diastolic and systolic volume according to the Simpson's biplane modified method of discs. However, Simpson's method cannot be applied to patients with poor echogenicity in the apical views and errors in image

plane positioning and geometric assumptions inherent in Simpson's method may limit the usefulness of two-dimensional echocardiography for evaluation of left ventricular volumes (18, 19). Transesophageal echocardiography is another method to determine AVA, but it is semi-invasive and not feasible in all patients (7). Besides, severe valvular calcification may prevent clear visualization of the orifice area (20).

CMR is an ideal technique for evaluation of ventricular volumes as it is independent of geometric assumptions, accurate, and reproducible (21). Combining measurements of stroke volume by CMR with measurements of VTI across the aortic valve by echocardiography in a hybrid approach takes advantage of the excellent accuracy and reproducibility of CMR while avoiding the problems associated with echocardiographic determination of LVOTd and LVOT flow.

There is growing evidence that CMR can be a valuable alternative to echocardiography for evaluation of aortic valve stenosis (10–13). However, the methods used in these studies differed from our approach. CMR planimetry of the aortic valve seems to be an accurate and reliable technique (10–12). In cases where heavy calcification and turbulent flow across the valve lead to difficulties in edge discrimination due to signal void, areas of signal void are treated as part of the leaflet (10, 12). This might not be appropriate in all cases. Velocity-encoded CMR is another promising technique (13). However, data on the usefulness of this technique for quantification of aortic stenosis are limited and until real-time flow recording becomes available, velocity aliasing might be a source of inefficiency in this method.

Measurement of ventricular volumes by CMR imaging has become a routine clinical modality. It can rapidly be performed by CMR technologists. The examination time is less than 15 minutes, and image analysis and determination of ventricular parameters will add another 20 minutes. Acquisition of transaortic VTI by echocardiography will take another 5 to 10 minutes, resulting in a total time of 40 to 45 minutes. As shown in this study, the hybrid approach had low variability and excellent reproducibility. Together with the favorable results shown for variability and reproducibility of transaortic VTI, the overall results for calculation of AVA by the hybrid approach were proportionately better than the results for the standard CE. Variability and reproducibility of our echocardiographic data were comparable to those reported in other recently published studies (6, 9). Bland-Altman analysis of our results indicates that the standard CE and the hybrid approach agree, exhibiting a mean difference near zero and a spread within 2 SD. More importantly, the vast majority of patients (90%) will be classified in the same category of severity by both methods. Only two patients were classified differently. Both had AVA close to 1 cm<sup>2</sup>.

#### 4.1. Limitations

Arrhythmias other than rate-controlled atrial fibrillation, severe mitral regurgitation, significant left-to-right shunting,

and general contraindications to CMR can limit the utility of this approach in clinical practice. Only few patients in this study had severe impairment of left ventricular function, and none of them had low gradient aortic valve stenosis. Therefore, the value of our approach in this subset of patients remains unclear.

## 5. Conclusion

The hybrid approach for calculation of AVA takes advantage of the excellent capabilities of CMR for determination of SV, while bypassing the difficulties associated with echocardiographic determination of LVOTd and LVOT flow. In patients with poor acoustic windows, heavy calcification of the aortic valve, or significant flow acceleration in the LVOT, this method can be a valuable alternative to the standard CE.

## Acknowledgment

This work was done without any financial support. The authors have no financial interest in this article.

## References

1. Zoghbi WA, Farmer KL, Soto JG, Nelson JG, Quinones MA. Accurate noninvasive quantification of stenotic aortic valve area by Doppler echocardiography. *Circulation* 1986; 73:452–459.
2. Oh JK, Taliencio CP, Holmes DR Jr, Reeder GS, Bailey KR, Seward JB, Tajik AJ. Prediction of the severity of aortic stenosis by Doppler aortic valve area determination: prospective Doppler-catheterization correlation in 100 patients. *J Am Coll Cardiol* 1988; 11:1227–1234.
3. 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; 7:509–517.
4. Skjaerpe T, Hegrenaes L, Hatle L. Noninvasive estimation of valve area in patients with aortic stenosis by Doppler ultrasound and two-dimensional echocardiography. *Circulation* 1985; 72:810–818.
5. Currie PJ, Hagler DJ, Seward JB, Reeder GS, Fyfe DA, Bove AA, Tajik AJ. Instantaneous pressure gradient: a simultaneous Doppler and dual catheter correlative study. *J Am Coll Cardiol* 1986; 7:800–806.
6. Dumont Y, Arsenault M. An alternative to standard continuity equation for the calculation of aortic valve area by echocardiography. *J Am Soc Echocardiogr* 2003; 16:1309–1315.
7. Tribouilloy C, Shen WF, Peltier M, Mirode A, Rey JL, Lesbre JP. Quantitation of aortic valve area in aortic stenosis with multiplane transesophageal echocardiography: comparison with monoplane transesophageal approach. *Am Heart J* 1994; 128:526–532.
8. Okura H, Yoshida K, Hozumi T, Akasaka T, Yoshikawa J. Planimetry and transthoracic two-dimensional echocardiography in noninvasive assessment of aortic valve area in patients with valvular aortic stenosis. *J Am Coll Cardiol* 1997; 30:753–759.
9. Smith LA, Cowell SJ, White AC, Boon NA, Newby DE, Northridge DB. Contrast agent increases Doppler velocities and improves reproducibility of aortic valve area measurements in patients with aortic stenosis. *J Am Soc Echocardiogr* 2004; 17:247–252.

10. Kupfahl C, Honold M, Meinhardt G, Vogelsberg H, Wagner A, Mahrholdt H, Sechtem U. Evaluation of aortic stenosis by cardiovascular magnetic resonance imaging: comparison with established routine clinical techniques. *Heart* 2004; 90:893–901.
11. Friedrich MG, Schulz-Menger J, Poetsch T, Pilz B, Uhlich F, Dietz R. Quantification of valvular aortic stenosis by magnetic resonance imaging. *Am Heart J* 2002; 144:329–334.
12. John AS, Dill T, Brandt RR, Rau M, Ricken W, Bachmann G, Hamm CW. Magnetic resonance to assess the aortic valve area in aortic stenosis: how does it compare to current diagnostic standards? *J Am Coll Cardiol* 2003; 42:519–526.
13. Caruthers SD, Lin SJ, Brown P, Watkins MP, Williams TA, Lehr KA, Wickline SA. Practical value of cardiac magnetic resonance imaging for clinical quantification of aortic valve stenosis: comparison with echocardiography. *Circulation* 2003; 108:2236–2243.
14. Ahmed S, Shellock FG. Magnetic resonance imaging safety: implications for cardiovascular patients. *J Cardiovasc Magn Reson* 2001; 3:171–182.
15. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986; 1:307–310.
16. Myreng Y, Molstad P, Endresen K, Ihlen H. Reproducibility of echocardiographic estimates of the area of stenosed aortic valves using the continuity equation. *Int J Cardiol* 1990; 26:349–359.
17. Zhou YQ, Faerstrand S, Matre K. Velocity distributions in the left ventricular outflow tract in patients with valvular aortic stenosis. Effect on the measurement of aortic valve area by using the continuity equation. *Eur Heart J* 1995; 16:383–393.
18. Gopal AS, Shen Z, Sapin PM, Keller AM, Schnellbaecher MJ, Leibowitz DW, Akinboboye OO, Rodney RA, Blood DK, King DL. Assessment of cardiac function by three-dimensional echocardiography compared with conventional noninvasive methods. *Circulation* 1995; 92:842–853.
19. Sapin PM, Schroder KM, Gopal AS, Smith MD, DeMaria AN, King DL. Comparison of two- and three-dimensional echocardiography with cineventriculography for measurement of left ventricular volume in patients. *J Am Coll Cardiol* 1994; 24:1054–1063.
20. Blumberg FC, Pfeifer M, Holmer SR, Kromer EP, Riegger GA, Elsner D. Quantification of aortic stenosis in mechanically ventilated patients using multiplane transesophageal Doppler echocardiography. *Chest* 1998; 114:94–97.
21. Pennell DJ. Ventricular volume and mass by CMR. *J Cardiovasc Magn Reson* 2002; 4:507–513.