

Automated quantitative assessment of cardiovascular magnetic resonance-derived atrioventricular junction velocities

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Leng S, Zhao XD, Huang FQ, Wong JI, Su BY, Allen JC, Kassab GS, Tan RS, Zhong L. Automated quantitative assessment of cardiovascular magnetic resonance-derived atrioventricular junction velocities. *Am J Physiol Heart Circ Physiol* 309: H1923–H1935, 2015. First published September 25, 2015; doi:10.1152/ajpheart.00284.2015.—The assessment of atrioventricular junction (AVJ) deformation plays an important role in evaluating left ventricular systolic and diastolic function in clinical practice. This study aims to demonstrate the effectiveness and consistency of cardiovascular magnetic resonance (CMR) for quantitative assessment of AVJ velocity compared with tissue Doppler echocardiography (TDE). A group of 145 human subjects comprising 21 healthy volunteers, 8 patients with heart failure, 17 patients with hypertrophic cardiomyopathy, 52 patients with myocardial infarction, and 47 patients with repaired Tetralogy of Fallot were prospectively enrolled and underwent TDE and CMR scan. Six AVJ points were tracked with three CMR views. The peak systolic velocity (Sm1), diastolic velocity during early diastolic filling (Em), and late diastolic velocity during atrial contraction (Am) were extracted and analyzed. All CMR-derived septal and lateral AVJ velocities correlated well with TDE measurements (Sm1: $r = 0.736$; Em: $r = 0.835$; Am: $r = 0.701$; Em/Am: $r = 0.691$; all $p < 0.001$) and demonstrated excellent reproducibility [intrastudy: $r = 0.921$ – 0.991 , intraclass correlation coefficient (ICC): 0.918 – 0.991 ; interstudy: $r = 0.900$ – 0.970 , ICC: 0.887 – 0.957 ; all $p < 0.001$]. The evaluation of three-dimensional AVJ motion incorporating measurements from all views better differentiated normal and diseased states [area under the curve (AUC) = 0.918] and provided further insights into mechanical dyssynchrony diagnosis in HF patients (AUC = 0.987). These findings suggest that the CMR-based method is feasible, accurate, and consistent in quantifying the AVJ deformation, and subsequently in diagnosing systolic and diastolic cardiac dysfunction.

atrioventricular junction deformation; cardiovascular magnetic resonance tissue doppler echocardiography; feature tracking

NEW & NOTEWORTHY

Cardiovascular magnetic resonance-derived atrioventricular junction (AVJ) velocities correlate significantly with tissue Doppler echocardiography measurements with no angle dependence and excellent reproducibility. AVJ velocities are valuable indexes of left ventricular systolic and diastolic function in patients with cardiovascular diseases.

THE ATRIOVENTRICULAR JUNCTION (AVJ) displacements and velocities are significant indicators of systolic and diastolic ventricular functions (4, 8, 25, 31). At present, available evidence suggest that systolic myocardial velocity at the

lateral mitral annulus (MA) is a measure of longitudinal systolic function and is correlated with measurements of left ventricular (LV) ejection fraction (EF) (10) and peak dP/dt (33). The measurement of early MA diastolic velocity can distinguish a pseudonormal from a normal diastolic filling pattern (26). Therefore, quantitative analysis of AVJ velocities and deformation has attracted great interest in recent years.

Tissue Doppler echocardiography (TDE) is a well-established technique that enables measurements of atrioventricular annular and regional myocardial velocities (19). The velocity curves obtained from TDE contain both timing and velocity data throughout the cardiac cycle. The most clinically useful data from the velocity curves are the positive peak systolic velocity (Sm1) and the two negative diastolic velocities, the first, occurring during early diastolic filling (Em), and the second, late diastolic tissue velocity (Am), occurring during atrial contraction (2). TDE measurements have limitations and pitfalls, however, that may affect accuracy and reproducibility. Proper sample volume placement at the annulus is critical to produce accurate tissue Doppler tracings. Subtle changes in sample volume positioning outside the annulus can greatly influence the Doppler tracings (13). In addition, TDE measures only the vector of motion that is parallel to the direction of the ultrasound beam similar to all Doppler techniques (14).

Cardiovascular magnetic resonance (CMR) offers an alternative noninvasive modality of choice for evaluation of cardiac anatomy, ventricular function (5), contractility (38), wall stress (39, 40), and regional area strain (29, 35). However, there still lacks simple, validated CMR technique to quantitatively measure the AVJ deformation. Previously, Saba et al. (23, 24) used a four-chamber cine view to calculate the lateral AVJ displacement. The correlation between mitral velocity early diastole and peak early diastolic velocity of the lateral MA from transthoracic echocardiography was $r = 0.362$ in 50 patients and $r = 0.624$ in a separate cohort of 27 patients. In their extended study (22), the same approach was applied to the septal and lateral AVJ analysis of 24 hypertrophic cardiomyopathy (HCM) and 14 normal subjects. In a very recent study, Wu et al. (32) examined the clinical potential of a CMR technique for quantifying global LV diastolic function, using volume tracking of the MA with cine CMR images.

Despite some recent advances, the quantification of AVJ deformation with CMR imaging remains a challenging task, mainly due to the large variation of AVJ motion and blurring artifacts in CMR images. Furthermore, the AVJ demonstrates an arc-like motion with longitudinal direction (toward the apex) and radial (toward the center of the MA) components

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(22). All existing CMR-based methods measured only the AVJ deformation along the longitudinal direction, ignoring those along the radial direction, which have clinical significance.

The goals of this study are 1) to assess the accuracy and reproducibility of a semiautomatic tracking system of AVJ deformation with CMR imaging. Compared with the AVJ tracking techniques with the same CMR modality reported previously (16, 32), improvements have been advanced in our tracking system to increase accuracy and reproducibility. The accuracy of AVJ velocities derived from the four-chamber long-axis CMR view will be compared with the measurements from TDE in healthy subjects and patients with various heart diseases, including HCM, heart failure (HF), myocardial infarction (MI), and repaired Tetralogy of Fallot (rTOF); and 2) to further evaluate the three-dimensional (3D) AVJ deformation and synchrony by incorporating measurements from two-, three-, and four-chamber CMR views.

MATERIALS AND METHODS

Study population. A group of 145 subjects was prospectively enrolled and underwent TDE and CMR scan. The subject selection was consecutive. Twenty one subjects were considered as normal in the absence of any LV and/or right ventricular dysfunction. The remaining 124 patients had HF, HCM, MI, or rTOF. Demographic and clinical characteristics of the population are listed in Table 1.

For all subjects, exclusion criteria were standard contraindications to TDE and CMR. Patients with atrial fibrillation or other arrhythmias were also excluded. The protocol was approved by the SingHealth centralized institutional review board, and informed consent was obtained from each participant.

TDE imaging. TDE was conducted by experienced sonographers using a digital commercial harmonic imaging ultrasound system with a 2.5-MHz phased-array transducer (Aloka $\alpha 10$). The tissue Doppler imaging was performed using pulse-wave Doppler with sample volume placing at the junction of the LV wall with the MA of the septal and lateral myocardial segments from the four-chamber view. The velocities, namely S_{m1} , E_m , and A_m , were derived from the TDE. The frame rate was between 80 and 100 frames/s. With the 2.5-MHz transducer and three cycles in each pulse-wave, the wavelength and spatial pulse length were given as 0.6 and 1.8 mm, respectively.

CMR imaging. The CMR scans were performed using steady-state free precession (SSFP) cine gradient echo sequences. All subjects

were imaged on a 1.5T Siemens scanner (Avanto; Siemens Medical Solutions, Erlangen, Germany) with a 12-element body matrix coil. SSFP end-expiratory breath hold cine images were acquired in multiplanar short- and long-axis views. Typical imaging parameters were as follows: TR/TE 34/1 ms, flip angle 47°, slice thickness 8 mm for both short and long axis, echo time 1.21 ms, repetition time 33.96 ms, pixel bandwidth 930 Hz, field of view 250–380 mm, temporal resolution ~ 35 ms, in-plane spatial resolution 1.6×1.6 – 1.8×1.8 mm, 40 frames/cardiac cycle for patients with HF and 25 for all other enrolled subjects.

Semiautomatic AVJ tracking. A software system was developed for semiautomatic tracking of AVJ deformation in two-, three-, and four-chamber long-axis CMR views (septal and lateral AVJs obtained from the 4-chamber view, anterosseptal and posterolateral AVJs obtained from the 3-chamber view, and anterior and posterior AVJs obtained from the 2-chamber view are shown in Fig. 1, A–C). The tracking system was developed using MATLAB (MathWorks) and used the method of matching-by-correlation, which has been applied in AVJ tracking in CMR (16, 32).

The matching-by-correlation method is a well-known object recognition and tracking algorithm (11). Given an image (called searching region here), the correlation problem is to find all places in the searching region that match a given subimage (also called a mask; masks at septal/anterosseptal/anterior and lateral/posterolateral/posterior AVJs are indicated in Fig. 1, A–C, with green and red rectangles). One approach for finding matches is to treat the mask as a spatial filter and compute the sum of products (or a normalized version of it) for each location of the mask in the searching region. Then the best match of the mask in the searching region is the location of the maximum value in the resulting correlation image.

The AVJ tracking system is semiautomatic and requires minimal manual intervention. The mask selection in the initial frame (or multiple-mask selection upon user setting) is the only user input. Thereafter, the algorithm automatically executes the adaptive feature tracking for all the subsequent frames. Hence, the intraobserver and interobserver variability is expected to be insignificant since operator dependence is relegated to variation only in site selection of AVJ. Compared with the presented work flow (16, 32), further improvements have been included in our tracking system to increase accuracy. Technical details can be found in APPENDIX A.

AVJ velocity and displacement extraction. Considering the equal clinical importance and significance of AVJ deformation along the longitudinal and radial directions, the AVJ velocity v_n was calculated based on the coordinates of the lower right corner of the masks at each frame throughout the cardiac cycle (Fig. 1, D–G):

Table 1. Demographics and clinical characteristics of the enrolled subjects

Variables	Normal (n = 21)	HF Patients (n = 8)	HCM Patients (n = 17)	MI Patients (n = 52)	rTOF Patients (n = 47)
Age, yr	40 $\pm$ 14	57 $\pm$ 12	54 $\pm$ 13	52 $\pm$ 9	36 $\pm$ 14
Gender, female/male	6/15	2/6	10/7	0/52	30/17
Weight, kg	65.6 $\pm$ 16.2	85.2 $\pm$ 22.4	69.7 $\pm$ 19.3	75.3 $\pm$ 16.1	63.3 $\pm$ 16.6
Height, cm	164.2 $\pm$ 11	165 $\pm$ 11.4	163 $\pm$ 11.9	169 $\pm$ 6.6	161 $\pm$ 9.1
BSA, m ²	1.77 $\pm$ 0.27	1.92 $\pm$ 0.32	1.77 $\pm$ 0.29	1.85 $\pm$ 0.22	1.67 $\pm$ 0.26
DBP, mmHg	71 $\pm$ 9	64 $\pm$ 2.2	73 $\pm$ 12.7	65 $\pm$ 8.7	69 $\pm$ 11.3
SBP, mmHg	120 $\pm$ 16	117 $\pm$ 13.1	133 $\pm$ 22.1	111 $\pm$ 15.2	120 $\pm$ 17.4
LVEDV, ml	135 $\pm$ 33	296 $\pm$ 93	140 $\pm$ 44	184 $\pm$ 46	128 $\pm$ 30
LVESV, ml	51 $\pm$ 18	245 $\pm$ 102	42 $\pm$ 23	103 $\pm$ 46	51 $\pm$ 17
LVEF, %	62 $\pm$ 7	18 $\pm$ 8	71 $\pm$ 9	46 $\pm$ 11	60 $\pm$ 7
LV mass index, g/m ²	56 $\pm$ 9	99 $\pm$ 17	102 $\pm$ 42	70 $\pm$ 14	57 $\pm$ 12
HR (CMR), beats/min	70 $\pm$ 10	80 $\pm$ 16	69 $\pm$ 17	72 $\pm$ 13	74 $\pm$ 13
HR (TDE), beats/min	72 $\pm$ 16	80 $\pm$ 18	67 $\pm$ 7	70 $\pm$ 11	68 $\pm$ 15

Values are means $\pm$ SD; n, no. of subjects. BSA, body surface area; DBP, diastolic blood pressure; SBP, systolic blood pressure; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; LVEF, left ventricular ejection fraction; LV, left ventricular; HR, heart rate; CMR, cardiac magnetic resonance; TDE, tissue Doppler echocardiography; HF, heart failure; HCM, hypertrophic cardiomyopathy; MI, myocardial infarction; rTOF, repaired Tetralogy of Fallot.

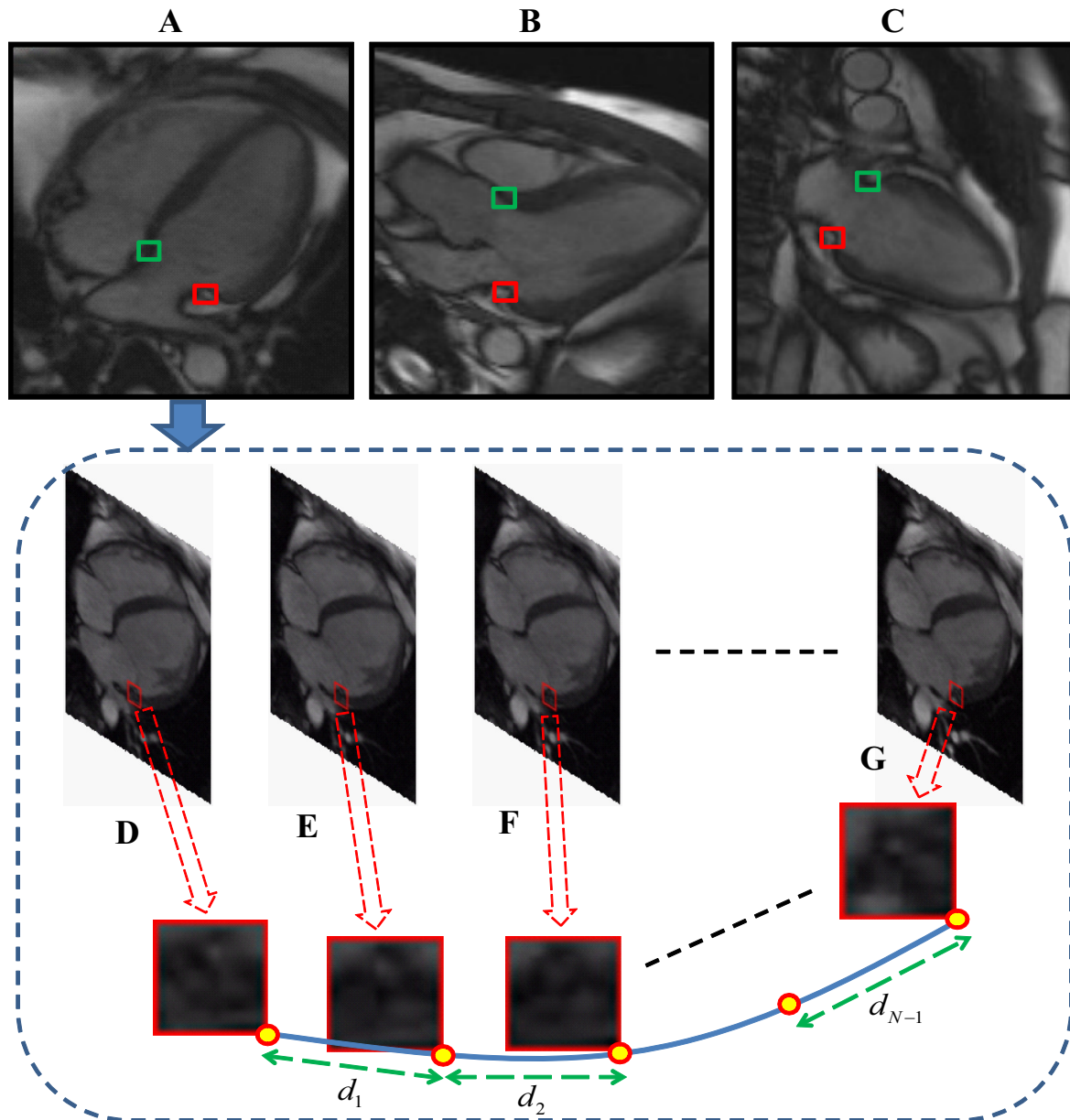


Fig. 1. Tracking of septal (green) and lateral (red) atrioventricular junction (AVJs) from an apical 4-chamber view (A), anteroseptal (green) and posterolateral (red) AVJs from an apical 3-chamber view (B), and anterior (green) and posterior (red) AVJs from an apical 2-chamber view (C). AVJ velocity calculation with 4-chamber cardiovascular magnetic resonance (CMR) imaging based on coordinates of the lower right corner of selected (updated) masks at frame 1 (D), frame 2 (E), frame 3 (F), and the last frame (G). d_n , Euclidean distance between the lower right corner points of the masks at two adjacent frames.

$$v_n = \frac{d_n}{\Delta t}, n = 1, \dots, N - 1$$

where N is the number of CMR frames, d_n is the Euclidean distance between the lower right corner points of updated masks at two adjacent frames, and Δt denotes the CMR effective image acquisition time. The AVJ displacements could be obtained by computing the cumulative integral of v_n via the trapezoidal method.

By convention, TDE velocities are positive if moving toward and negative if moving away from the transducer. In our CMR-based method, the AVJ velocity at each frame was defined to be positive if the AVJ is moving away from and negative if moving toward that at the start of systole (i.e., the first frame). The Sm1 is the dominant velocity above the baseline, starting shortly after the QRS complex of

electrocardiography. Em and Am are the two main velocities that are usually seen below the baseline (15). The Sm1, Em, and Am were automatically extracted from the AVJ velocity curve by searching for the dominant positive and negative peaks.

Statistical analysis. The accuracy of the tracking algorithm was assessed by an expert cardiologist through visually checking the output video. The Pearson's r correlation and Bland-Altman analysis were used to assess the linear relationships and agreements between the AVJ velocities derived from CMR and TDE.

To evaluate the reproducibility of the method, intraobserver and interobserver variability were studied for a randomly chosen subgroup of 10 cases (10 septal, 10 lateral) using the Pearson's r correlation, Bland-Altman analysis, and intraclass correlation coefficient (ICC). For interobserver variability study, the analysis was repeated by a second inde-

pendent observer using the system, blinded to the first observer's results. For intraobserver variability study, the analysis was repeated by the same observer who reanalyzed the same 10 cases after 3 days.

RESULTS

The semiautomatic tracking process requires <1 min/AVJ point (on average), including loading input CMR video, selecting mask and searching region, tracking and velocities extraction, saving data, and visual confirmation of video outputs. Analysis was feasible in all subjects.

AVJ motion tracking and velocity extraction. Our system successfully tracked the AVJ motions and extracted the AVJ velocities for all the subjects enrolled in the study.

Figure 2A depicts the segmented trueFISP two-dimensional CMR image frames of the four-chamber view at the start of systole, end systole, diastasis, and end of diastole for the AVJ tracking of one 35-yr-old male healthy volunteer. The masks for septal and lateral AVJs are indicated with the green and red rectangles. Figure 2, B and C, shows the computed myocardial velocity curves in septal and lateral AVJs. Three obvious peaks (one positive and two negative) exist in each resulting curve corresponding to Sm1, Em, and Am. Moreover, a zone of very low velocity can be observed during the diastolic slow-filling phase. The extracted values of Sm1, Em, and Am in septal were 6.3, 10.0, and 7.1 cm/s, and those in lateral were 10.3, 16.5, and 8.5 cm/s, respectively.

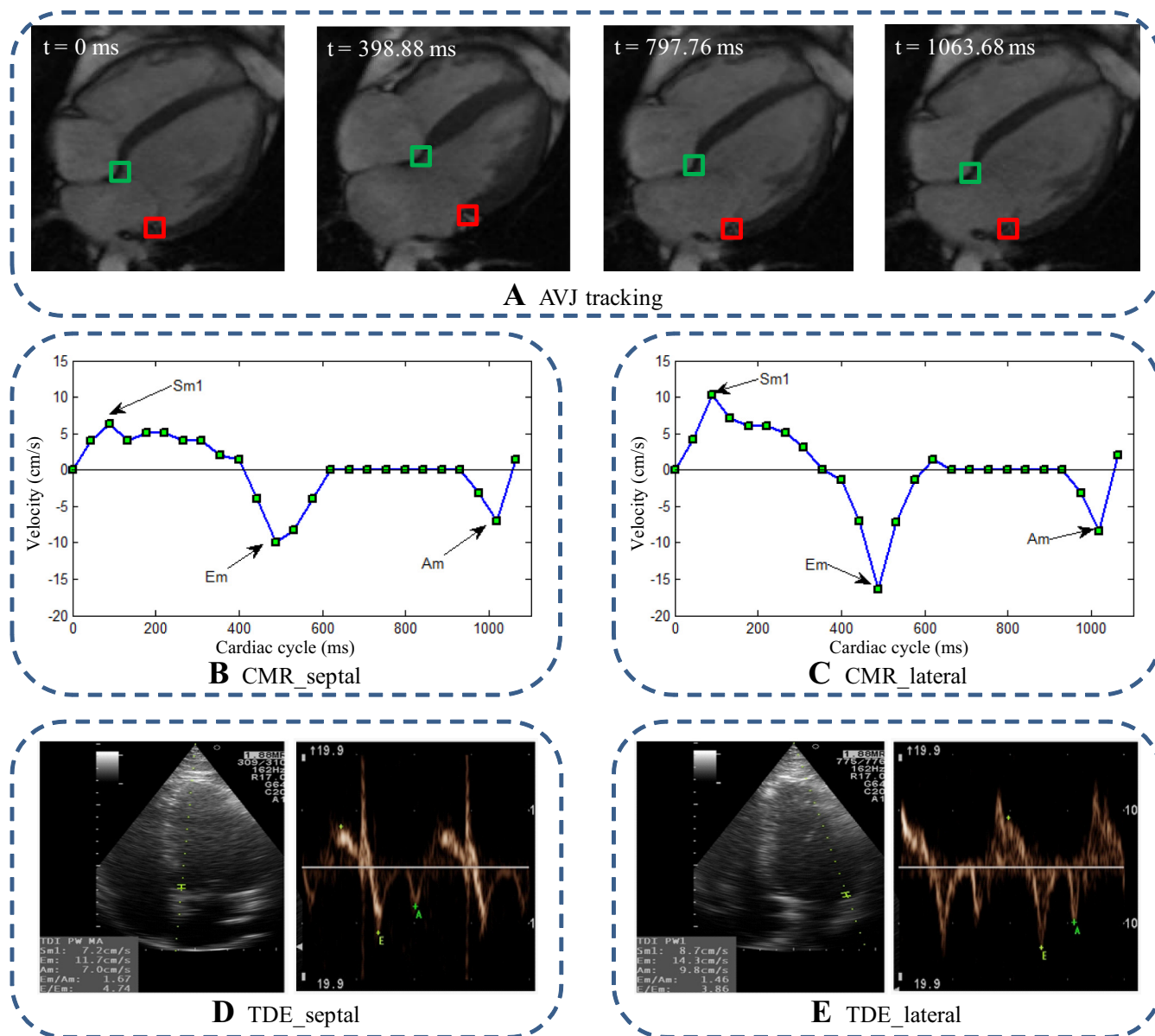


Fig. 2. For one 35-yr-old male healthy volunteer: AVJ tracking indicated by segmented trueFISP 2-dimensional 4-chamber CMR frames at the start of systole (0 ms), end systole (398.9 ms), diastasis (797.8 ms), and end diastole (1,063.7 ms) (A). The masks for septal and lateral AVJs are indicated with the green and red rectangles. The CMR-derived AVJ velocities using our system are displayed in B and C, wherein the values of Sm1, Em, and Am in septal are 6.3, 10.0, and 7.1 cm/s, and that in lateral are 10.3, 16.5, and 8.5 cm/s, respectively. Tissue Doppler echocardiography (TDE)-derived AVJ velocities are shown in D and E, wherein the values of Sm1, Em, and Am in septal are 7.2, 11.7, and 7 cm/s, and that in lateral are 8.7, 14.3, and 9.8 cm/s, respectively.

Figure 3, *B* and *C*, shows the tracking results of septal and lateral AVJs for one 69-yr-old male patient with HF. The extracted Sm1, Em, and Am in septal and lateral were 2.3, 2.4, and 1.4 cm/s and 4.1, and 4.9, 3.1 cm/s, respectively.

Noise is inherent to displacement, and subsequently the velocity measurements. The analysis on the effect of noise on tracking accuracy can be found in APPENDIX B, where the results demonstrated low variation between the “clean” and “noisy” measurements with excellent correlation and narrow limits of error.

Comparison with TDE. The AVJ velocities derived from four-chamber CMR view were compared with those obtained with TDE. As two examples, the tracking results for the above-mentioned healthy volunteer and HF patient were

compared with TDE measurements. Figure 2, *D* and *E*, shows images from TDE for the healthy volunteer where sample volumes indicated by green marks were placed at the septal and lateral AVJs. The TDE-derived AVJ velocities are also shown in Fig. 2, *D* and *E*, wherein the values of Sm1, Em, and Am in septal were 7.2, 11.7, and 7 cm/s, and those in lateral were 8.7, 14.3, and 9.8 cm/s. Likewise, the obtained septal and lateral AVJ velocities from TDE for the HF patient were 3.0, 2.2, and 2.6 cm/s and 4.6, 6.8, and 4 cm/s, as indicated in Fig. 3, *D* and *E*.

The same procedures were executed on all enrolled subjects, and the results were analyzed on a statistical basis. Table 2 describes the CMR- and TDE-derived septal and lateral AVJ velocities for all groups, and Fig. 4 shows the relation of results

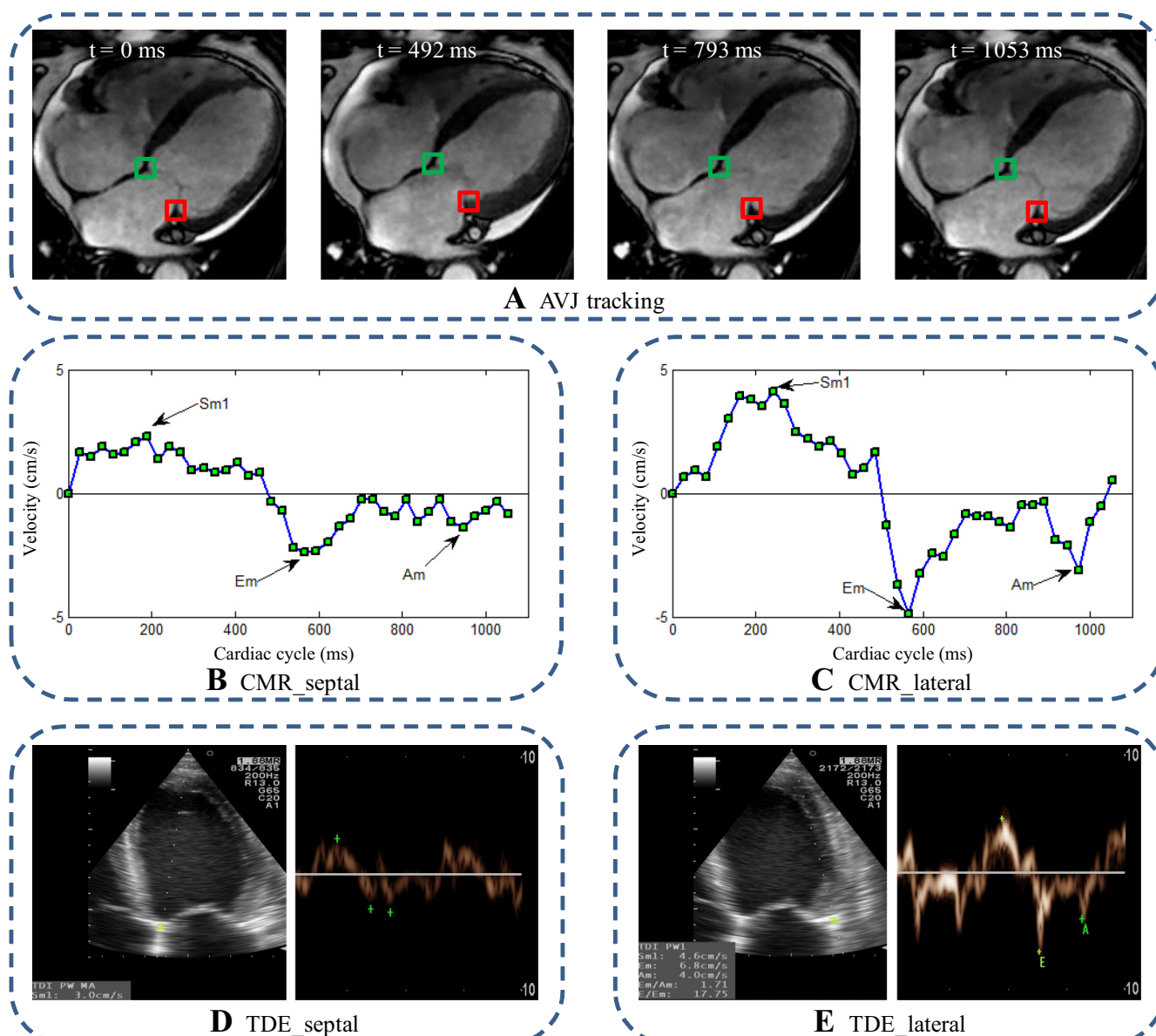


Fig. 3. For one 69-yr-old male HF patient: AVJ tracking indicated by segmented trueFISP 2-dimensional 4-chamber CMR frames at the start of systole (0 ms), end systole (492 ms), diastasis (793 ms), and end diastole (1,053 ms) (A). The masks for septal and lateral AVJs are indicated with the green and red rectangles. The CMR-derived AVJ velocities using our system are displayed in *B* and *C*, wherein the values of Sm1, Em, and Am in septal are 2.3, 2.4, and 1.4 cm/s, and that in lateral are 4.1, 4.9, and 3.1 cm/s, respectively. The TDE-derived AVJ velocities are shown in *D* and *E*, wherein the values of Sm1, Em, and Am in septal are 3, 2.2, and 2.6 cm/s, and that in lateral are 4.6, 6.8, and 4 cm/s, respectively.

Table 2. CMR- and TDE-derived septal and lateral AVJ velocities

Modality	AVJ Velocity	Normal (n = 21)	HF Patients (n = 8)	HCM Patients (n = 17)	MI Patients (n = 52)	rTOF Patients (n = 47)	HF, HCM, and MI Patients (n = 77)
CMR	Sm1_septal, cm/s	7.3 ± 1.1	3.9 ± 1.5*	6.2 ± 1.4*	6.2 ± 1.5*	6.7 ± 1.7	5.9 ± 1.6*
	Em_septal, cm/s	9.6 ± 2.5	3.0 ± 0.8*	5.0 ± 1.9*	6.3 ± 2.1*	9.5 ± 3.1	5.7 ± 2.2*
	Am_septal, cm/s	6.7 ± 1.6	3.0 ± 1.7*	4.8 ± 1.7*	6.3 ± 2.2	5.3 ± 1.4*	5.7 ± 2.3*
	Em/Am_septal	1.6 ± 0.6	1.3 ± 0.7	1.1 ± 0.4*	1.1 ± 0.4*	2.0 ± 0.9	1.1 ± 0.4*
	Sm1_lateral, cm/s	9.8 ± 1.6	5.1 ± 1.4*	6.2 ± 1.5*	7.3 ± 2.1*	8.7 ± 2.2*	6.8 ± 2.0*
	Em_lateral, cm/s	13.0 ± 3.0	4.6 ± 1.6*	6.6 ± 2.3*	8.6 ± 2.7*	13.0 ± 4.1	7.8 ± 2.8*
	Am_lateral, cm/s	7.9 ± 3.3	4.5 ± 2.8*	5.1 ± 2.4*	6.9 ± 2.8	6.2 ± 2.4*	6.3 ± 2.9*
	Em/Am_lateral	2.0 ± 1.0	1.3 ± 0.7	1.6 ± 0.9	1.5 ± 0.7*	2.4 ± 1.1	1.5 ± 0.8*
TDE	Sm1_septal, cm/s	8.7 ± 1.4	4.2 ± 1.3*	6.5 ± 1.3*	6.7 ± 1.3*	7.5 ± 1.4*	6.4 ± 1.5*
	Em_septal, cm/s	10.7 ± 3.0	5.0 ± 2.6*	5.5 ± 1.8*	7.0 ± 1.9*	10.5 ± 2.9	6.5 ± 2.1*
	Am_septal, cm/s	8.6 ± 2.2	4.9 ± 2.0*	6.6 ± 2.3*	7.7 ± 2.4	6.8 ± 1.5*	7.2 ± 2.4*
	Em/Am_septal	1.4 ± 0.7	1.1 ± 0.5	0.9 ± 0.4*	1.0 ± 0.4*	1.6 ± 0.6	1.0 ± 0.4*
	Sm1_lateral, cm/s	10.4 ± 2.0	4.9 ± 0.7*	6.3 ± 1.6*	6.8 ± 1.9*	9.0 ± 2.0*	6.5 ± 1.8*
	Em_lateral, cm/s	13.9 ± 3.3	6.3 ± 1.7*	7.4 ± 3.8*	8.7 ± 2.7*	15.1 ± 4.1	8.2 ± 3.0*
	Am_lateral, cm/s	9.1 ± 2.9	5.5 ± 2.4*	6.6 ± 3.0*	7.9 ± 2.9	7.6 ± 2.1*	7.4 ± 3.0*
	Em/Am_lateral	1.8 ± 0.8	1.3 ± 0.5	1.3 ± 0.6	1.3 ± 0.6*	2.2 ± 0.8	1.3 ± 0.6*

Values are means ± SD; n, no. of subjects. AVJ, atrioventricular junction; Sm1, peak systolic velocity; Em, diastolic velocity during early diastolic filling; Am, late diastolic velocity during atrial contraction. The last column presents results for the cohort of patients with HF, HCM, and MI. Also given is the comparison of median AVJ velocities between normal volunteers and every patient group with *denoting statistically significant difference ($P < 0.05$).

between the two modalities. All CMR-derived AVJ velocities correlated well with TDE (Table 3,) and the overall correlations were $r = 0.736, 0.835, 0.701$, and 0.691 ($p < 0.001$) for Sm1, Em, Am, and Em/Am, respectively. All patient groups demonstrated statistically significant differences in the CMR-derived AVJ velocities (Table 2) compared with healthy volunteers.

Projected CMR-derived velocity measurements. The AVJ velocity at each CMR frame was calculated along the displacement vector of the tracked AVJ points between the current and preceding frames, taking into account the radial component of the AVJ motion. Table 4 presents the CMR-derived septal and lateral AVJ velocities projected along the longitudinal and radial directions. As shown in Table 4, the proportion of the projected septal AVJ velocity along the radial direction became larger compared with that in normal controls in the presence of heart dysfunction.

Relationship between CMR-derived Sm1 and LVEF. In all participants except HCM patients, the curvilinear relationship [$\text{LVEF} = -0.955(\text{Sm1})^2 + 19.13(\text{Sm1}) - 33.33$, $r = 0.724$; Fig. 5A] was found between LVEF and the mean CMR-derived peak systolic velocities Sm1 of septal and lateral AVJs. The instantaneous rate of change (27) of LVEF with respect to Sm1 at $\text{Sm1} = \text{Sm1}'$ was $-1.91(\text{Sm1}') + 19.13$; and the average rate of change (27) of LVEF that results from a unit change in Sm1 over the entire interval was $\approx 5\%$.

When the value of CMR-derived peak systolic velocity at lateral AVJ was used to assess the global LV systolic function, a cut-off point of <7.7 cm/s identified diseased states (excluding rTOF) with an area under the receiver-operating characteristic (ROC) curve (AUC) of 0.866, sensitivity of 90.5%, and specificity of 70.1% (Fig. 5B), demonstrating higher diagnostic accuracy than that using LVEF (AUC = 0.730, sensitivity = 81.0%, and specificity = 65.8% with cut-off LVEF of 50%).

Three-dimensional analyses and synchrony. The CMR-derived velocities at anterior/posterior (from the 2-chamber view) and anteroseptal/posterolateral (from the 3-chamber view) AVJs are presented in Table 5, together with septal/lateral (from the 4-chamber view) and the six-point mean AVJ velocities by CMR. Similar to the

observation from Fig. 5A, the results shown in Fig. 5C reveal the curvilinear relationship ($r = 0.760$) between LVEF and the six-point mean CMR-based Sm1. The ROC analysis (Fig. 5B) demonstrated that the six-point average Sm1 better differentiated diseased states from normal (AUC = 0.918 compared with Sm1 at lateral and posterolateral AVJs with AUC = 0.866 and 0.899, and LVEF with AUC = 0.730).

The AVJ velocity data from the three CMR views were reconstructed to provide insights into mechanical dyssynchrony. Table 6 presents the results of a subanalysis of data in HF patients and controls. As indicated in Table 6, the patients in the HF group had significantly larger standard deviations of time-to-peak Sm1 and Em (denoted by TSm1-6pt-SD and TEm-6pt-SD), indicating a dyssynchronous AVJ motion in HF patients. The standard deviation of time-to-peak Am (TAm-6pt-SD) tended to increase in HF patients compared with the control group, although the difference did not reach statistical significance. Figure 5D demonstrates the excellent diagnostic performance of TSm1-6pt-SD and TEm-6pt-SD with AUC = 0.987 and 0.932, respectively, in differentiating HF from normal.

Reproducibility. Table 7 shows the results of intraobserver and interobserver reproducibility analysis. The CMR-derived AVJ velocities demonstrated good to excellent consistency in terms of Pearson's correlation ($r = 0.991, 0.989$, and 0.921 for intrameasurements and $r = 0.970, 0.947$, and 0.900 for intermeasurements of Sm1, Em, and Am, respectively) and ICC (ranges from 0.887 to 0.991) with no significant bias and narrow limits of agreement for both intraobserver ($0.061 \pm 0.336, 0.024 \pm 1.029$, and 0.166 ± 1.674 cm/s for Sm1, Em, and Am, respectively) and interobserver ($0.053 \pm 0.739, 0.021 \pm 2.21$, and -0.246 ± 1.907 cm/s for Sm1, Em, and Am, respectively) measurements.

DISCUSSION

The current study yielded several important findings. First, we implemented a semiautomatic CMR-based AVJ tracking

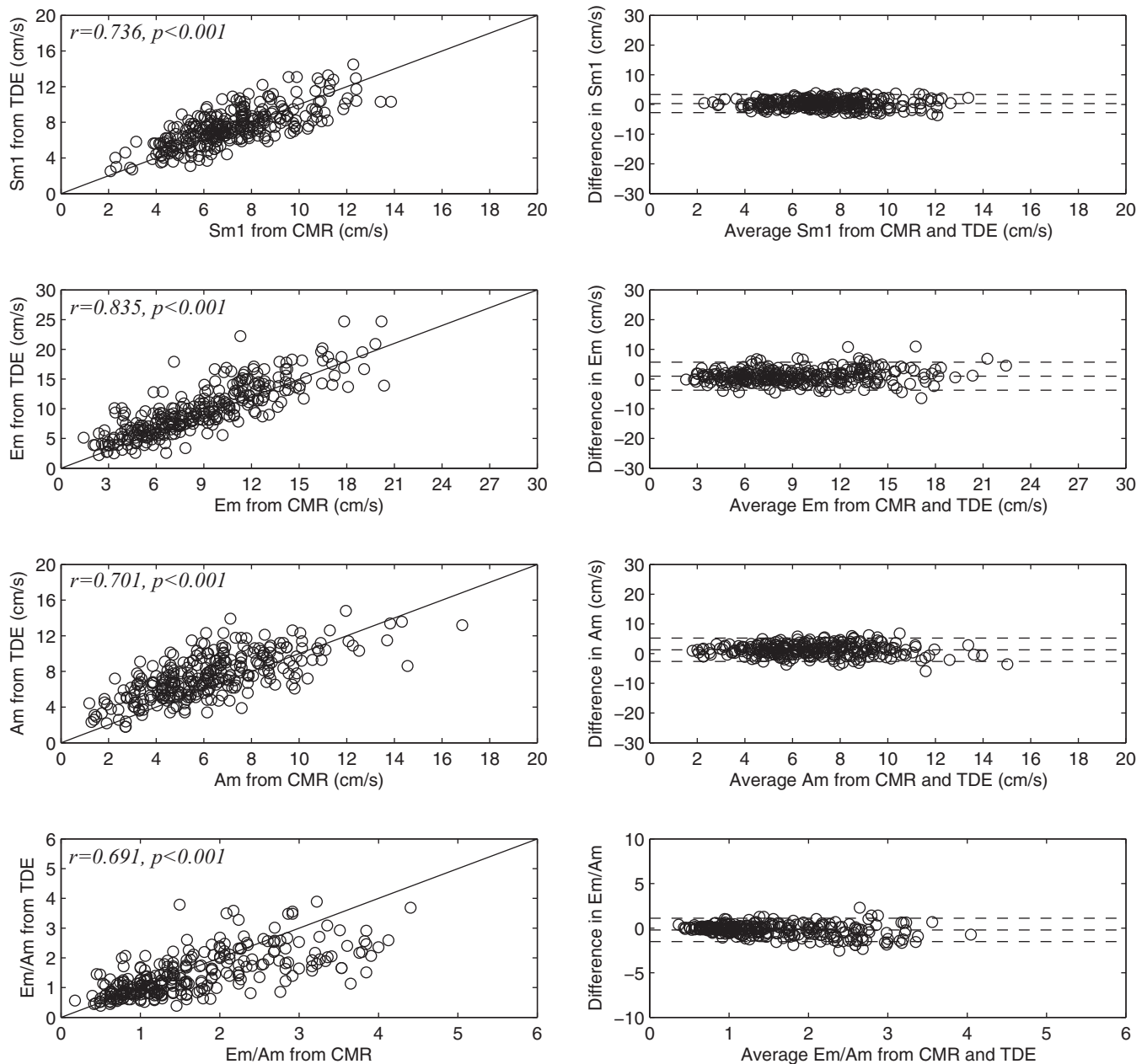


Fig. 4. Agreement of CMR- and TDE-derived AVJ velocities. *Left*, correlation between CMR-derived and TDE-derived Sm1, Em, Am, and Em/Am. *Right*, agreement between CMR-derived and TDE-derived Sm1, Em, Am, and Em/Am using Bland-Altman analysis.

system with high robustness and short processing duration. Second, we applied the technique in normal volunteers and patients with various heart diseases and demonstrated that the CMR-derived AVJ velocities conformed to the typical features

Table 3. Correlation strength of the CMR-derived AVJ velocities with those obtained by TDE

	Correlation r		
	Septal	Lateral	Overall
Sm1	0.708*	0.738*	0.736*
Em	0.794*	0.829*	0.835*
Am	0.683*	0.710*	0.701*
Em/Am	0.699*	0.661*	0.691*

*Statistical significance ($P < 0.001$).

of AVJ deformation. Good correlations were achieved between the AVJ velocities obtained from the CMR and TDE. Third, the good diagnostic performance and high reproducibility made this CMR-based method reliable for use in clinical practice and research.

Technical aspects of study. The semiautomatic AVJ tracking was performed using the well-known matching-by-correlation method, which has been a classical approach to the problems of locating and recognizing an object in an image (11). It uses a mask, tailored to a specific feature of the search image, that is to be detected. The correlation output will be highest at places where the search image structure matches the mask structure. This method is normally implemented by first picking out a part of the search image to use as the mask.

Table 4. CMR-derived septal and lateral AVJ velocities projected along longitudinal and radial directions

Direction	AVJ Velocity	Normal (n = 21)	HF Patients (n = 8)	HCM Patients (n = 17)	MI Patients (n = 52)	rTOF Patients (n = 47)
Longitudinal	Sm1_septal, cm/s	7.1 ± 1.1 (97 ± 5)	3.4 ± 1.3 (88 ± 12)	5.8 ± 1.3 (93 ± 11)	5.9 ± 1.6 (95 ± 7)	6.5 ± 1.6 (96 ± 4)
	Em_septal, cm/s	9.4 ± 2.4 (99 ± 1)	2.3 ± 1.4 (71 ± 32)	4.8 ± 2.0 (96 ± 9)	6.1 ± 2.2 (96 ± 13)	9.2 ± 3.0 (97 ± 4)
	Am_septal, cm/s	6.5 ± 1.6 (98 ± 3)	2.4 ± 1.5 (88 ± 9)	4.8 ± 2.2 (93 ± 11)	6.1 ± 2.4 (95 ± 9)	4.9 ± 1.5 (96 ± 5)
	Sm1_lateral, cm/s	9.0 ± 1.4 (92 ± 5)	4.3 ± 2.2 (82 ± 33)	5.7 ± 1.9 (91 ± 17)	6.7 ± 2.0 (92 ± 8)	8.1 ± 2.3 (93 ± 11)
	Em_lateral, cm/s	12.6 ± 3.2 (95 ± 6)	4.2 ± 1.9 (89 ± 21)	6.2 ± 2.6 (93 ± 18)	8.3 ± 2.8 (95 ± 10)	12.4 ± 3.9 (96 ± 6)
Radial	Am_lateral, cm/s	7.0 ± 2.4 (88 ± 9)	3.6 ± 2.2 (83 ± 32)	4.4 ± 2.3 (90 ± 14)	5.9 ± 2.6 (83 ± 18)	5.1 ± 2.3 (83 ± 20)
	Sm1_septal, cm/s	1.4 ± 1.2 (19 ± 14)	1.7 ± 1.2 (42 ± 23)	2.1 ± 1.9 (29 ± 22)	1.5 ± 1.2 (25 ± 19)	1.5 ± 1.0 (22 ± 13)
	Em_septal, cm/s	1.3 ± 0.9 (14 ± 9)	1.4 ± 0.8 (54 ± 36)	0.9 ± 1.0 (20 ± 21)	1.0 ± 0.8 (19 ± 18)	2.0 ± 1.4 (22 ± 14)
	Am_septal, cm/s	1.1 ± 0.8 (17 ± 11)	1.1 ± 0.8 (41 ± 23)	1.3 ± 1.1 (28 ± 22)	1.4 ± 1.0 (24 ± 19)	1.0 ± 0.8 (21 ± 15)
	Sm1_lateral, cm/s	3.6 ± 1.7 (35 ± 15)	2.0 ± 1.3 (40 ± 28)	1.6 ± 1.4 (27 ± 25)	2.4 ± 1.6 (33 ± 20)	2.5 ± 2.0 (28 ± 22)
	Em_lateral, cm/s	3.6 ± 1.8 (28 ± 15)	1.3 ± 1.0 (30 ± 30)	1.4 ± 1.5 (23 ± 25)	1.9 ± 1.3 (23 ± 19)	3.1 ± 2.6 (23 ± 18)
	Am_lateral, cm/s	3.8 ± 2.6 (44 ± 17)	2.4 ± 3.5 (34 ± 36)	1.8 ± 1.5 (37 ± 22)	3.6 ± 2.8 (47 ± 25)	2.9 ± 2.2 (44 ± 26)

Values are means ± SD in cm/s; n, no. of subjects. Values in parentheses denote percentage proportion of projected velocity component.

The mask selection is the most critical step in applying matching-by-correlation to AVJ tracking. A proper selection of mask can largely increase the tracking accuracy and consistency. The physiological deformations of the surrounding area of the AVJ point (especially the lateral AVJ point) are quite complex and different among human subjects. In addition, the

limited CMR imaging quality and blurring artifacts make the AVJ tracking even more challenging.

Some general guidelines on the mask selection were provided in this study. High system accuracy and stability were achieved without losing significant standardization. First, the AVJ point should be included in the mask area,

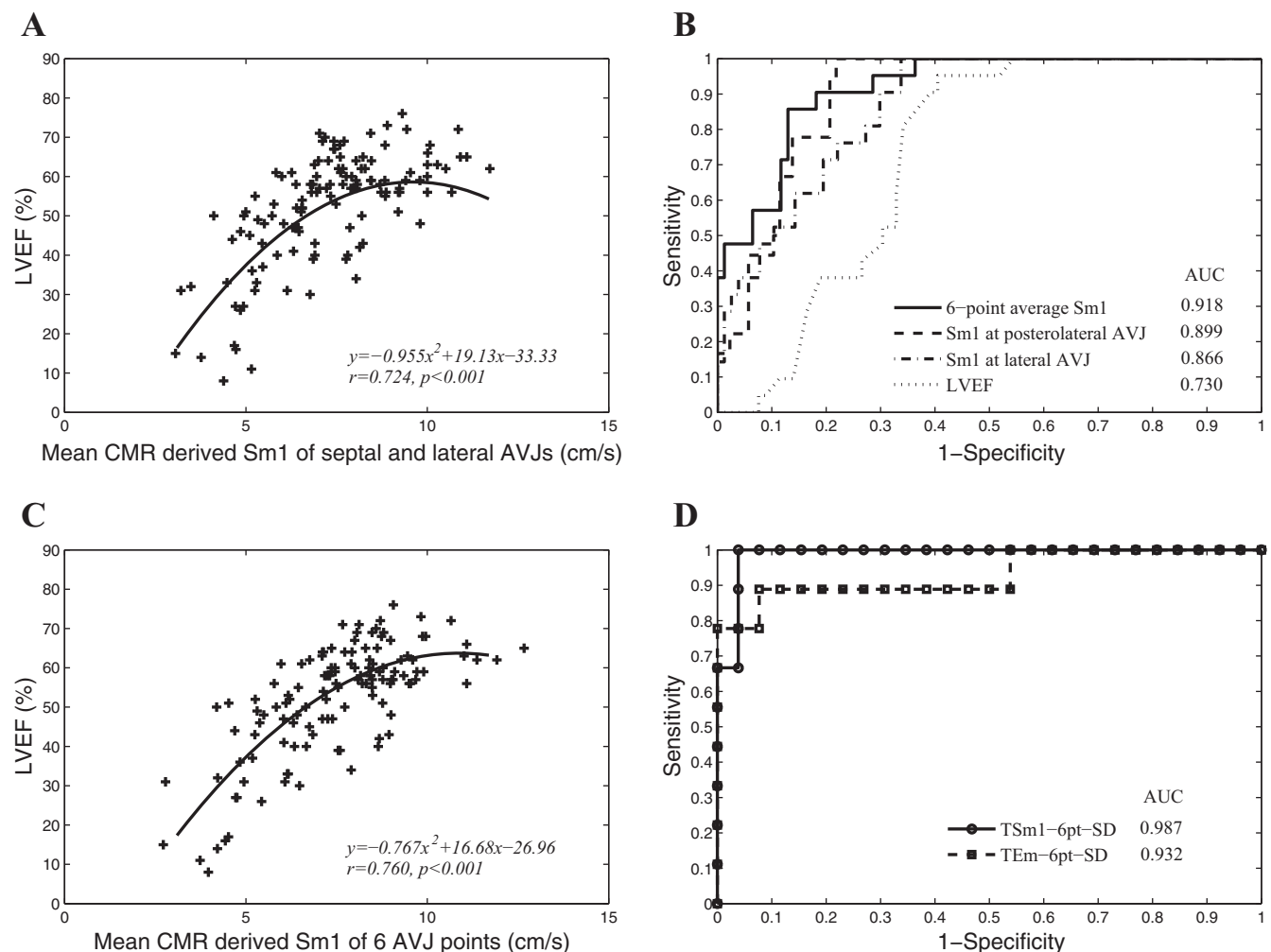


Fig. 5. A: relationship between left ventricle ejection fraction (LVEF) and mean CMR-derived Sm1 of septal and lateral AVJs. B: area under the receiver-operating characteristic (ROC) curve of CMR-derived 6-point average Sm1, Sm1 at lateral AVJ, Sm1 at posterolateral AVJ, and LVEF to detect diseased states. C: relationship between LVEF and mean CMR-derived Sm1 of 6 AVJ points. D: area under the ROC of CMR-derived TSm1-6pt-SD (SD of time-to-Sm1) and TEm-6pt-SD (SD of time-to-Em) to detect dyssynchrony in heart failure (HF) patients.

Table 5. CMR-derived AVJ velocities in three dimensions

AVJ Velocity	Normal (n = 21)	HF Patients (n = 8)	HCM Patients (n = 17)	MI Patients (n = 52)	rTOF Patients (n = 47)	HF, HCM, and MI Patients (n = 77)
Sm1_anterior, cm/s	7.8 ± 1.5	3.1 ± 0.9*	5.8 ± 1.3*	5.8 ± 1.5*	7.8 ± 2.0	5.5 ± 1.6*
Em_anterior, cm/s	9.9 ± 2.3	3.3 ± 0.8*	5.5 ± 1.6*	6.4 ± 1.9*	11.0 ± 3.7	5.9 ± 2.0*
Am_anterior, cm/s	7.7 ± 3.5	3.8 ± 2.1*	5.5 ± 2.7*	6.6 ± 2.4	7.1 ± 2.2	6.1 ± 2.5
Em/Am_anterior	1.7 ± 1.2	1.1 ± 0.5	1.2 ± 0.7	1.1 ± 0.5*	1.7 ± 0.8	1.1 ± 0.6
Sm1_posterior, cm/s	10.6 ± 2.1	4.4 ± 1.7*	7.3 ± 2.4*	7.8 ± 2.3*	9.4 ± 2.8	7.3 ± 2.4*
Em_posterior, cm/s	11.7 ± 2.9	3.1 ± 0.7*	6.4 ± 3.3*	7.0 ± 2.7*	11.2 ± 4.3	6.5 ± 3.0*
Am_posterior, cm/s	10.0 ± 3.7	5.4 ± 3.6*	7.7 ± 3.9*	8.2 ± 3.3*	7.6 ± 2.5*	7.9 ± 3.5*
Em/Am_posterior	1.4 ± 0.7	0.8 ± 0.6	1.0 ± 0.6	1.0 ± 0.6*	1.6 ± 0.7	1.0 ± 0.6*
Sm1_anteroseptal, cm/s	7.7 ± 1.1	3.7 ± 1.3*	6.8 ± 2.3	6.1 ± 1.5*	7.1 ± 1.9	6.0 ± 1.9*
Em_anteroseptal, cm/s	8.2 ± 2.1	3.4 ± 1.5*	5.3 ± 1.8*	5.4 ± 1.6*	6.7 ± 1.9*	5.1 ± 1.7*
Am_anteroseptal, cm/s	5.8 ± 1.1	2.6 ± 1.3*	4.3 ± 1.5*	5.0 ± 1.5*	3.8 ± 1.3*	4.6 ± 1.6*
Em/Am_anteroseptal	1.5 ± 0.6	1.5 ± 0.6	1.4 ± 0.7	1.2 ± 0.4*	1.9 ± 0.8*	1.2 ± 0.5
Sm1_posterolateral, cm/s	10.2 ± 1.9	4.9 ± 1.3*	6.7 ± 1.9*	7.2 ± 2.0*	9.3 ± 2.4	6.8 ± 2.0*
Em_posterolateral, cm/s	12.7 ± 2.8	3.9 ± 1.9*	6.2 ± 2.3*	7.8 ± 2.6*	12.1 ± 4.6	7.0 ± 2.7*
Am_posterolateral, cm/s	9.3 ± 3.1	4.4 ± 2.8*	6.8 ± 2.8*	6.8 ± 2.9*	6.9 ± 2.8*	6.6 ± 2.9*
Em/Am_posterolateral	1.6 ± 0.7	1.1 ± 0.8	1.1 ± 0.7	1.4 ± 0.8	2.0 ± 1.2	1.3 ± 0.8
Sm1_septal, cm/s	7.3 ± 1.1	3.9 ± 1.5*	6.2 ± 1.4*	6.2 ± 1.5*	6.7 ± 1.7	5.9 ± 1.6*
Em_septal, cm/s	9.6 ± 2.5	3.0 ± 0.8*	5.0 ± 1.9*	6.3 ± 2.1*	9.5 ± 3.1	5.7 ± 2.2*
Am_septal, cm/s	6.7 ± 1.6	3.0 ± 1.7*	4.8 ± 1.7*	6.3 ± 2.2	5.3 ± 1.4*	5.7 ± 2.3*
Em/Am_septal	1.6 ± 0.6	1.3 ± 0.7	1.1 ± 0.4*	1.1 ± 0.4*	2.0 ± 0.9	1.1 ± 0.4*
Sm1_lateral, cm/s	9.8 ± 1.6	5.1 ± 1.4*	6.2 ± 1.5*	7.3 ± 2.1*	8.7 ± 2.2*	6.8 ± 2.0*
Em_lateral, cm/s	13.0 ± 3.0	4.6 ± 1.6*	6.6 ± 2.3*	8.6 ± 2.7*	13.0 ± 4.1	7.8 ± 2.8*
Am_lateral, cm/s	7.9 ± 3.3	4.5 ± 2.8*	5.1 ± 2.4*	6.9 ± 2.8	6.2 ± 2.4*	6.3 ± 2.9*
Em/Am_lateral	2.0 ± 1.0	1.3 ± 0.7	1.6 ± 0.9	1.5 ± 0.7*	2.4 ± 1.1	1.5 ± 0.8*
Sm1_6pt_mean, cm/s	8.8 ± 0.8	4.1 ± 0.8*	6.6 ± 1.6*	6.7 ± 1.5*	8.2 ± 1.8*	6.4 ± 1.6*
Em_6pt_mean, cm/s	10.9 ± 2.2	3.5 ± 1.0*	5.9 ± 1.9*	6.8 ± 1.9*	10.5 ± 3.0	6.3 ± 2.1*
Am_6pt_mean, cm/s	7.6 ± 2.3	3.7 ± 2.1*	5.8 ± 2.3*	6.6 ± 2.1	6.1 ± 1.7*	6.1 ± 2.3*
Em/Am_6pt_mean	1.6 ± 0.7	1.2 ± 0.6	1.2 ± 0.5*	1.1 ± 0.4*	1.9 ± 0.8	1.1 ± 0.5*

Values are means ± SD; n, no. of subjects. The last column presents results for the cohort of patients with HF, HCM, and MI. The last four rows give the 6-point average results. Also given is the comparison of median AVJ velocities between normal volunteers and every patient group with *denoting statistically significant difference ($P < 0.05$).

and the mask should have a small size such that the moving trajectory of the mask is close enough to that of the AVJ point. The purpose of doing so is to maintain the clinical relevance of the tracking results. Second, the mask image should have features that are apparent enough to support the feature matching. Such distinctive features within the mask guarantee that the point being tracked is nearly identical in the next time frame. Third, those surrounding areas of the AVJ with large deformation should be excluded from the mask to achieve low tracking errors. Following these guidelines and visual inspections of the CMR video inputs, the masks and searching regions were selected for all of the CMR data, and good to excellent success rates of tracking were achieved. For instance, 93% (135 out of 145) of the

septal AVJ were successfully tracked at first attempt albeit 86% (124 out of 145) for the lateral AVJ. The slightly lower first-attempt success rate for the lateral AVJ is due to its more complex and rapidly changing deformation. To address this and further increase the tracking accuracy, multiple-mask selection became an option where the operator can select the masks at uniformly or nonuniformly distributed intermediate frames. Each of these masks became a starting point to be detected in subsequent frames until the frame containing the next mask was reached.

To evaluate the tracking quality of the system, we proposed the following three ways. First, the resulting AVJ velocity and displacement curves must conform to the typical features of AVJ deformation. Generally speaking, three obvious peaks corresponding to Sm1, Em, and Am should be visible. The AVJ displacement should demonstrate an upward trend followed by a downward trend. Second, the tracking quality can be well assessed by visually checking the output video, which shows the motion and trajectory of the tracked AVJ. Third, the location of the updated mask in the last frame should be close to that of the selected mask in the initial frame, ensuring a low cumulative tracking error. This is reasonable since the AVJ tends to move back to its original location after a complete cardiac cycle.

TDE has been a widely used technique to measure peak myocardial velocities and is considered to be well suited to the measurement of long-axis ventricular motion (14). However, one limitation of TDE and all previous CMR-based

Table 6. LV synchrony analysis in normal controls and HF patients

Variables	Normal (n = 21)	HF (n = 8)
TSm1, ms	115 ± 23	150 ± 50*
TEm, ms	503 ± 33	560 ± 66*
TAm, ms	857 ± 98	809 ± 73*
TSm1-6pt-SD, ms	14 ± 7	45 ± 20*
TEm-6pt-SD, ms	16 ± 8	41 ± 15*
TAm-6pt-SD, ms	22 ± 10	35 ± 24

Values are means ± SD; n, no. of subjects. TSm1, time-to-peak systolic velocity Sm1; TEm, time-to-peak velocity Em during early diastolic filling; TAm, time-to-peak velocity Am during atrial contraction; SD of TSm1 (TSm1-6pt-SD), TEm (TEm-6pt-SD), and TAm (TAm-6pt-SD) derived from 6 AVJ points from 2-, 3-, and 4-chamber long-axis CMR images. *Statistically significant difference ($P < 0.05$).

Table 7. Results of intraobserver and interobserver reproducibility analysis, in terms of Pearson's correlation coefficient, bias in Bland-Altman analysis, and ICC

	Intraobserver (cases = 10)			Interobserver (cases = 10)		
	<i>r</i>	Bias	ICC (95% CI)	<i>r</i>	Bias	ICC (95% CI)
Sm1	0.991	0.061 (−0.274 to 0.397)	0.991 (0.977–0.996)	0.970	0.053 (−0.715 to 0.822)	0.957 (0.895–0.983)
Em	0.989	0.024 (−1.005 to 1.053)	0.988 (0.970–0.995)	0.947	0.021 (−2.189 to 2.231)	0.942 (0.859–0.976)
Am	0.921	0.166 (−1.508 to 1.840)	0.918 (0.804–0.967)	0.900	−0.246 (−2.153 to 1.661)	0.887 (0.736–0.954)

ICC, intraclass correlation coefficient; CI, confidence interval.

methods (22–24, 32) is that the AVJ deformation along the radial direction was ignored. The radial AVJ motion should provide significant clinical information in assessing LV systolic and diastolic functions, especially for patients with severe cardiac dysfunction because the major component of AVJ motion does not necessarily lie in the longitudinal direction in the presence of heart disease. Hence, the rationale for the use of true AVJ velocities was adopted in our study to take into account the radial component of the AVJ motion.

Clinical aspects of study. Available evidence shows that the peak AVJ velocities Sm1, Em, and Am are valuable measures of overall LV contraction and relaxation (10). In this study, we developed methods to automatically extract the AVJ velocities from CMR sequences. Our findings indicate that the CMR-derived AVJ motion parameters have good clinical implications in assessing LV systolic and diastolic functions.

In clinical practice, there is parity between echocardiography and CMR in assessment of ventricular systolic function, but CMR lags echocardiography for evaluation of ventricular diastolic function, mainly because TDE and Doppler measurements are considered as the mainstay of evaluation of the ventricular diastolic function. Our study is a step toward achieving this parity. The study is clinically important because of the following reasons: 1) validation of CMR-derived AVJ measurements based on TDE gold standard; 2) comparison between normal subjects and subjects with various forms of cardiac disease that is clinically useful for establishing a range of normal values for clinical application; and 3) establishment of feasibility and efficacy of practical application of the proposed CMR-based method in the clinical setting.

In all enrolled control subjects, the mean CMR-derived systolic Sm1, diastolic Em and Am, and the Em/Am ratio at septal and lateral locations were 8.52 ± 1.87 cm/s, 11.30 ± 3.25 cm/s, 7.27 ± 2.62 cm/s, and 1.78 ± 0.85 , respectively, which were consistent with the normal values previously reported using TDE (6, 7). For the enrolled patients with various heart diseases, these mean CMR-derived measurements at septal and lateral AVJs were 4.50 ± 1.53 cm/s, 3.86 ± 1.52 cm/s, 3.79 ± 2.37 cm/s, and 1.30 ± 0.66 in HF patients, 6.16 ± 1.46 cm/s, 5.80 ± 2.25 cm/s, 4.97 ± 2.06 cm/s, and 1.34 ± 0.72 in HCM patients, and 6.72 ± 1.88 cm/s, 7.47 ± 2.65 cm/s, 6.59 ± 2.52 cm/s, and 1.26 ± 0.61 in MI patients, which were mostly in agreement with the previously presented TDE-derived value ranges (1, 3, 20). Studies investigating the AVJ velocities in rTOF patients are rare, and our CMR-derived values were 7.68 ± 2.18 cm/s, 11.19 ± 3.98 cm/s, 5.74 ± 2.00 cm/s, and $2.16 \pm$

0.99. Our results demonstrated three noteworthy points. First, our method was applicable to patients with various types of heart diseases. Second, general decreases in the systolic Sm1, diastolic Em and Am, and Em/Am ratio were observed in patients with HF, HCM, and MI, indicating impaired systolic and diastolic performance in all three exposed groups compared with controls. This finding was in line with that observed on TDE in patients with heart dysfunction (17). Third, the rTOF patients had significantly lower Sm1 and Am, comparable Em, and significantly higher Em/Am than healthy subjects.

AVJ velocity gives high diagnostic value and incremental predictive power for cardiac morbidity and mortality (30). The excellent agreement of the CMR-derived results with those obtained from TDE makes CMR a useful alternative tool to quantify the AVJ deformation for LV systolic and diastolic function assessment. One advantage of CMR imaging, compared with echocardiography and other imaging modalities, is its excellent myocardial tissue characterization (9). Moreover, the CMR-based method measures AVJ motion in both the longitudinal and radial directions, thus overcoming the limitation of angle dependency of TDE.

The LVEF is an important determinant of the severity of systolic heart dysfunction. In our study, the curvilinear relationship was found between LVEF and the CMR-derived peak systolic velocity Sm1 (Fig. 5, A and C), which was similar to the previously presented results (28). In addition, the Sm1 has shown better diagnostic power compared with LVEF. It has been demonstrated in earlier studies that patients with valvular heart diseases, hypertensive heart diseases, and HCM tend to have impaired systolic function despite preserved LVEF (21, 28, 34). In the current study, we also found decreased AVJ motion values derived from CMR in HCM patients even though their LVEF values were normal. Hence, LVEF alone does not always reliably reflect the severity of systolic dysfunction in all heart diseases, for example, HF with preserved EF (36, 37).

The techniques were also applied to perform the AVJ tracking in two- and three-chamber CMR views. The tracking of both longitudinal and radial velocity data in time, and over three orthogonal views, provided further insights on the cardiac mechanics. The evaluation of 3D motion parameters that represented a global score incorporating measurements from all views better differentiated normal and diseased states (Fig. 5B). Moreover, the assessment of ventricular mechanical dyssynchrony from 3D CMR (Table 6 and Fig. 5D) may be useful for future guidance of resynchronization therapy.

There were limitations to this study, including a small sample size of enrolled HF patients. In addition, the tem-

poral resolution of CMR is markedly lower compared with echocardiographic techniques. The practical implication is that CMR may miss an image frame that represents the point of peak velocity and therefore could systematically underestimate peak velocities compared with TDE with a higher temporal resolution. Indeed, this consistent underestimation is observed in Table 2, although the level of underestimation does not appear to be clinically relevant. Third, interstudy reproducibility is important in evaluating the robustness and clinical usefulness of any analytical techniques. The CMR has shown excellent interstudy reproducibility for LV function parameters (12, 18), which suggests that CMR is reliable for LV assessment. Future work will need to address whether this approach can quantify the AVJ motion with low interstudy variability. Fourth, the comparison of CMR-based AVJ velocities and displacements with peak dp/dt should also be conducted in the future, since dp/dt is an important parameter to measure the LV global contractility. Finally, a complete clinical applicability study on the AVJ deformation stratified by gender, age, and other patient characteristics remains a laudable goal for the future.

APPENDIX A

Detailed discussion on semiautomatic AVJ tracking. Given a $(2h + 1) \times (2w + 1)$ mask t and the searching region x , the matching by correlation is conducted by computing the normalized cross correlation at the location (u, v) :

$$c(u, v) = \frac{\sum_{i=-h}^h \sum_{j=-w}^w X(i, j)T(i, j)}{\sqrt{\sum_{i=-h}^h \sum_{j=-w}^w X(i, j)^2} \sqrt{\sum_{i=-h}^h \sum_{j=-w}^w T(i, j)^2}}$$

where

$$X(i, j) = x(u + i, v + j) - \bar{x}, \quad T(i, j) = t(u + i, v + j) - \bar{t}$$

and $\bar{x}$ and $\bar{t}$ denote the mean value of x and t , respectively.

Figure 6 gives the procedure of applying matching by correlation in AVJ tracking in CMR. The user selects the mask in frame 1 (red rectangle in Fig. 6A) and the searching region in frame 2 (blue rectangle in Fig. 6B) using the mouse to click and drag. The matching-by-correlation method is applied to find the best match of the mask in the searching region (Fig. 6, C and D). The point for best match becomes the lower right corner point of the updated mask in frame 2 that undergoes the same matching by correlation within the extracted searching region in frame 3. The same procedure is automatically executed iteratively for all subsequent frames.

The proper selections of the mask and searching region are the most critical steps in the AVJ tracking procedure. In Ref. 32, a square mask centered at the AVJ point was initially selected in the first frame. The sizes of the square mask in the initial frame and the searching region in the subsequent frames were chosen to be 20×20 pixels (10×10 pixels in Ref. 16) and 40×40 pixels (20×20 pixels in Ref. 16), respectively. The advantage of this approach was that it provided an easier way for the operator to select the mask and thus reduced the training duration. However, a square mask centered at the AVJ point with fixed size may not always be a suitable choice to achieve high tracking accuracy,

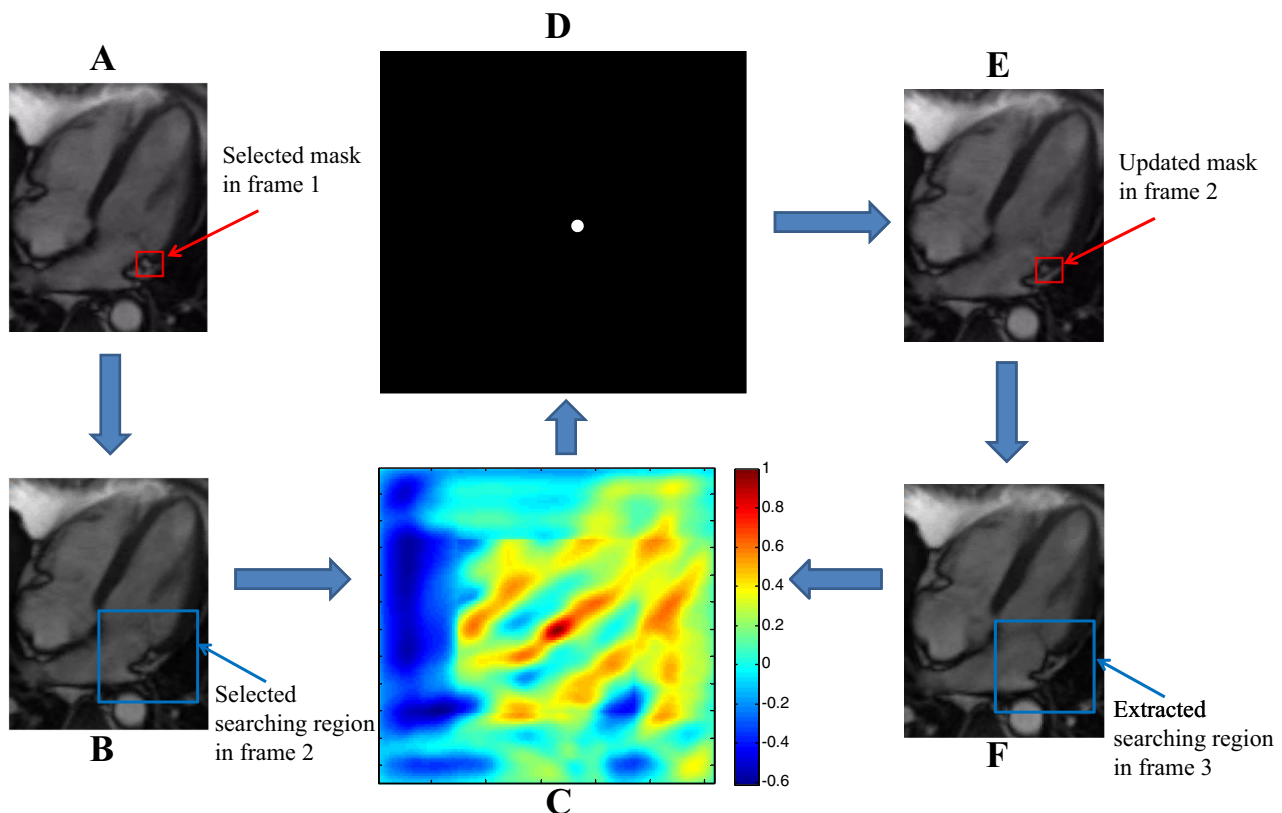


Fig. 6. Workflow of the AVJ tracking system: select the mask in frame 1 (the size of the mask remains the same in all subsequent frames) (A), select the searching region in frame 2 (the size of the searching region remains the same in all subsequent frames) (B), perform matching by correlation (C), locate the point for the best match (D), update the mask in frame 2 (E), and extract the searching region in frame 3 (F).

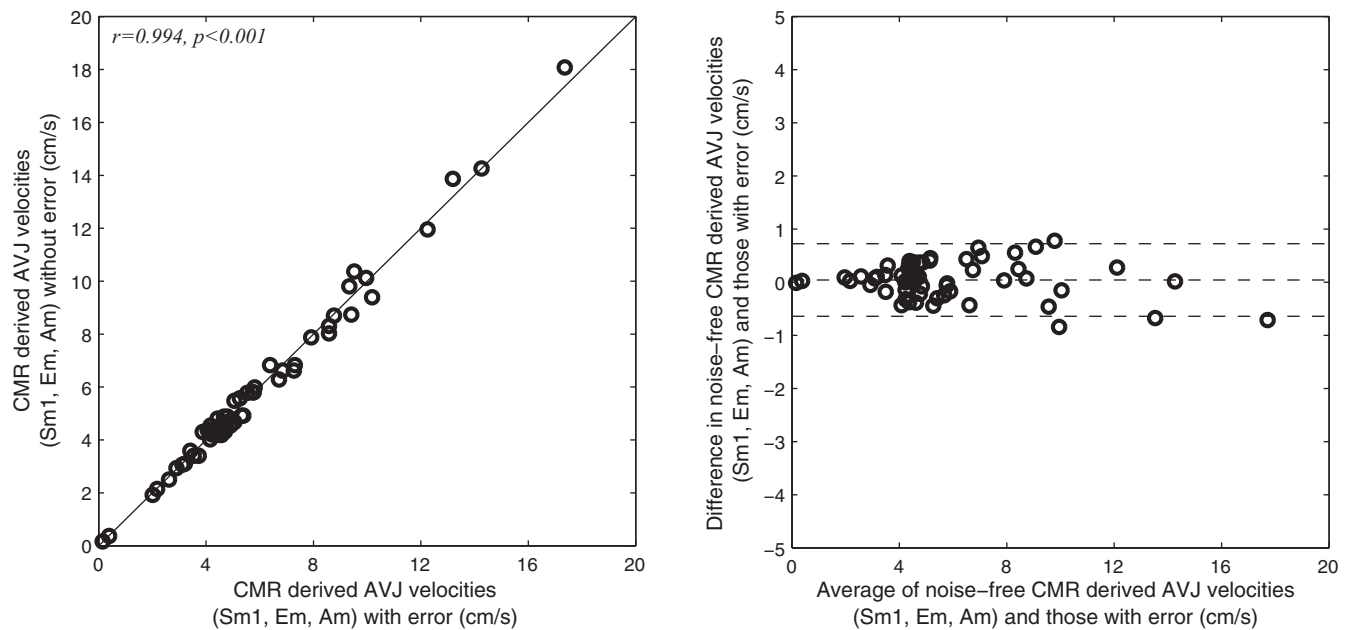


Fig. 7. Comparison of original and noisy CMR-derived velocities. *Left*, correlation plot; *right*, agreement plot using Bland-Altman analysis.

especially for the tracking of lateral AVJ. This is due to the fact that, first in some cases, the surrounding area around the AVJ point towards certain direction deforms in a very different way with respect to the AVJ point, and this part of the surrounding area should be excluded from the mask. Second, the masks with different sizes are needed for different cases, depending on the physiological shapes of the AVJ area.

Hence, instead of using the methods described previously (16, 32), we performed the mask and searching region selections by careful visual inspections according to the guidelines given below.

Guidelines for mask selection. The guidelines for mask selection are as follows: 1) the AVJ point is included in the mask area; 2) the mask has a small size such that the moving trajectories of the mask and the AVJ point are close enough; 3) the object inside the selected mask possesses distinctive features (e.g., in shapes) compared with the surrounding area; and 4) the deformation of the object inside the selected mask is small to achieve low tracking errors.

Guidelines for searching region selection. The guidelines for searching region selection are as follows: 1) the center of the searching region is close to the center of the selected mask; 2) the searching region covers all possible moving locations of the selected mask; and 3) the size of the searching region should not be too big to have short computational time.

Another challenge of applying the method of matching by correlation in AVJ tracking is that the variations of the physiological shapes for some AVJ areas are too large to be successfully tracked. To tackle this, our AVJ tracking system provides the option to select different mask numbers. The purpose of this option is to reduce the cumulative tracking error and to prevent the target loss throughout the tracking procedure. When the mask number is set to be 1, the tracking process becomes the same as that shown in Fig. 6. When the mask number is chosen to be greater than 1, the user can select multiple masks at the initial frame as well as intermediate uniformly or nonuniformly distributed frames throughout the cardiac cycle. Hence, the system provides a correction capability with user-selected multiple masks. The same matching-by-correlation procedures are applied to the frames in between the intermediate frames used for mask selection.

APPENDIX B

Effect of noise on tracking accuracy. Noise is inherent to displacement measurements. To evaluate the tracking accuracy in the presence of noise, artificial errors were added to the original distance measure-

ments between tracked AVJs at adjacent frames. The procedures for the generation of noisy distances and the subsequent velocity extraction are described below.

For each of the original Euclidean distances between adjacent tracked AVJs denoted as d_n , an error Δd_n was randomly generated between $-0.1d_n$ and $+0.1d_n$, i.e., the maximum distance error is 10%. The velocity was then calculated using $v_n = (d_n + \Delta d_n)/\Delta t$, where Δt is the CMR effective image acquisition time.

The procedure was executed on a subset of patients and normal controls with two subjects in each category. Figure 7 shows low variation between the original and noisy results with $r = 0.994$ and narrow limits of error (0.0413 ± 0.683 cm/s).

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

Author contributions: S.L., R.-S.T., and L.Z. conception and design of research; S.L., X.-D.Z., F.-Q.H., J.-I.W., B.-Y.S., and L.Z. performed experiments; S.L., X.-D.Z., F.-Q.H., J.-I.W., B.-Y.S., J.C.A., and L.Z. analyzed data; S.L., X.-D.Z., F.-Q.H., J.-I.W., B.-Y.S., and L.Z. interpreted results of experiments; S.L., X.-D.Z., and L.Z. prepared figures; S.L. and L.Z. drafted manuscript; S.L., J.C.A., G.S.K., R.-S.T., and L.Z. edited and revised manuscript; S.L., X.-D.Z., F.-Q.H., J.-I.W., B.-Y.S., J.C.A., G.S.K., R.-S.T., and L.Z. approved final version of manuscript.

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