

Research Article

Noninvasive Detection of Left-Ventricular Systolic Dysfunction by Acoustic Cardiography in Atrial Fibrillation

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Received 13 August 2010; Accepted 30 September 2010

Academic Editor: Filippos Triposkiadis

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Objectives. Assessment of left ventricular (LV) systolic function in patients with atrial fibrillation can be difficult. Acoustic cardiography provides several parameters for quantifying LV systolic function. We evaluated the ability of acoustic cardiography to detect LV systolic dysfunction in patients with and without atrial fibrillation. **Design.** We studied 194 patients who underwent acoustic cardiography and cardiac catheterization including measurement of angiographic ejection fraction (EF) and maximum LV dP/dt. LV systolic dysfunction was defined as LV maximum dP/dt < 1600 mmHg/s. Acoustic cardiographic parameters included electromechanical activation time (EMAT) and the systolic dysfunction index (SDI). **Results.** Acoustic cardiography detected systolic dysfunction with high specificity and moderate sensitivity with similar performance to EF (sensitivity/specification without afib: EMAT 30/96, SDI 40/90, EF at 35% 30/96; sensitivity/specification with afib: EMAT 64/82, SDI 59/100, EF at 35% 45/82). **Conclusions.** Acoustic cardiology can be used for diagnosis of LV systolic dysfunction in atrial fibrillation.

1. Introduction

Atrial fibrillation is a highly prevalent arrhythmia, particularly in patients with heart failure. Atrial fibrillation significantly increases with age in patients with heart failure, and the prevalence increases from <10% in those with New York Heart Association (NYHA) functional class I to almost 50% in those patients with NYHA class IV [1, 2]. It is estimated that two-thirds of patients with heart failure are over 65 years old and 4.5 times more likely to have atrial fibrillation in men and 5.9 times more likely in women [3]. Assessing systolic function in atrial fibrillation is especially important since both pharmacological and device-based therapies exist. However, due to the beat-to-beat variations in preload with atrial fibrillation, assessment of left ventricular systolic function is difficult. Systolic function is most commonly assessed using the ejection fraction (EF) measured by angiographic, echocardiographic, or radionuclide methods with varying success as schemas continue to be developed to improve accuracy during atrial fibrillation [4–6]. In addition,

invasive or imaging technologies such as cardiac magnetic resonance to quantify systolic function are expensive and not always readily available.

Acoustic cardiography (Audicor, Inovise Medical, Inc., Beaverton, OR) records and algorithmically interprets simultaneous digital ECG and acoustic data by using the same array of electrodes used for a standard ECG. However, in the V3 and V4 positions, it employs dual sensors that acquire both ECG and sound data. Measuring systolic time intervals and diastolic heart sounds, acoustic cardiography allows reliable assessment of hemodynamics [7–10]. Parameters produced by this technique include those to assess systolic function [11] including EMAT (electrical mechanical activation time, Q wave onset to the S1 interval), the presence of a third heart sound (S3), and SDI (systolic dysfunction index, a combination of EMAT, S3, QRS duration and QR interval). This diagnostic method is particularly appropriate in environments, where echocardiography or invasive assessment of LV function is not available [12] or when serial measurements are desired.

The goal of the present paper was to evaluate the use of acoustic cardiography as a rapid, noninvasive method to assess LV systolic dysfunction (LVSD) in a population with atrial fibrillation that also underwent invasive diagnostic evaluation. We tested the hypothesis that acoustic cardiography could discriminate those patients with and without LV dysfunction independent of whether or not they also had atrial fibrillation.

2. Materials and Methods

2.1. Subjects. The local Medical Ethics Committee approved the study. After obtaining written informed consent from each patient, we evaluated a convenience sample of 194 patients who underwent diagnostic cardiac catheterization. Patients were without food for at least 6 hours. Short-acting diuretics were withheld on the morning of the catheterization but other cardiac drugs were administered as usual.

All the subjects had measurement of left-ventricular EF and LV end-diastolic pressure (LVEDP). Left-ventricular maximum dP/dt (i.e., LV max(dP/dt)) was measured using a manometer-tipped catheter (Volcano Inc., Parker, TX, USA) in 108 patients and a fluid-filled catheter in the remaining 86. LV max(dP/dt) was calculated automatically (Schwarzer GmbH Medical Equipment, Munich, Germany) in normally conducted beats. Only recordings with a minimum of at least 4 normally conducted beats were used including in patients with atrial fibrillation. Values of LV max(dP/dt) of <1600 mmHg/s were considered to be a marker of LVSD [13–15]. Left ventricular ejection fraction was calculated using monoplane ventriculography. Measurements of right atrial, right ventricular and pulmonary artery systolic and wedge pressures were performed with multipurpose catheters.

2.2. Acoustic Cardiography. Acoustic cardiography data were recorded immediately prior to cardiac catheterization with the patient in a supine position. This quantitative method provides parameters for assessing both systolic and diastolic LV function. In the present study, we evaluated two systolic parameters—the electromechanical activation time (EMAT) and the systolic dysfunction index (SDI). EMAT measures the time interval from the onset of the QRS complex to the point of maximum intensity of the first heart sound. Therefore, EMAT indicates the amount of time required for the LV to generate sufficient force to close the mitral valve and reflects the velocity of force generated during systole. The SDI combines EMAT, QRS duration, QR interval and the strength of the third heart sound into one parameter (SDI = transform (QRS duration * QR interval * S3 strength * EMAT/RR interval)). The SDI value undergoes a nonlinear transformation and is then reported as a value between 0 and 10, where SDI > 5 indicates systolic dysfunction defined as EF < 50%, and SDI > 7.5 indicates EF < 35% and elevated filling pressure. The SDI was developed on separate learn and test sets of invasive cardiac catheterization data that provided both EF and LV end-diastolic pressure. The acoustic cardiographic parameters are calculated from a 10-second recording of data that typically involves averaging

of measurements from 8 to 12 beats. We hypothesized that EMAT and SDI could be used to detect LVSD.

2.3. Statistical Analysis. Data are presented as mean values and standard deviations with minimum and maximum values as ranges for continuous variables. Categoric data are presented as exact numbers and proportions. We tested the null hypothesis for continuous data using the unpaired T-test for patients with and without atrial fibrillation and a priori chose alpha <0.05 to indicate statistical significance. We also generated ROC curves to determine the diagnostic sensitivities and specificities for LVSD and to calculate positive and negative likelihood ratios. Unlike positive and negative predictive values, positive and negative likelihood ratios are independent of the prevalence of the abnormality in the population being tested [16]. To avoid dividing by zero, we set the positive likelihood ratio equal to sensitivity in the cases in which specificity was 100%.

3. Results

There were a total of 194 subjects recruited for this study. The mean age of the 155 subjects without atrial fibrillation was 62.6 ± 11.8 years (range: 22 to 86 years), and 102 (66%) of the subjects were men, whereas the mean age of the 39 patients with atrial fibrillation was 67.3 ± 10.7 years (range: 43 to 85 years) and 32 (82%) were men.

One hundred three (66%) of the subjects without atrial fibrillation had LVSD (a LV max(dP/dt) < 1600 mmHg/s), while 22 (56%) of the subjects with atrial fibrillation had LVSD. In the population without atrial fibrillation, the LV max(dP/dt) was 1474 ± 479 mmHg/s (range: 480 to 2928 mmHg/s) and 1589 ± 534 mmHg/s (range: 648 to 2832 mmHg/s) in the group with atrial fibrillation. Table 1 shows that the subjects with LVSD had significantly lower mean values of EF, larger end-diastolic and end-systolic volumes, and greater mean values of EMAT and the systolic dysfunction index. Heart rate was significantly higher and EMAT longer in the populations with atrial fibrillation independent of whether there was LVSD or not.

Figure 1 shows the means and 95% confidence intervals of EMAT, the systolic dysfunction index and EF. In both the patients with and without atrial fibrillation, EMAT and the systolic dysfunction index discriminate between the presence versus the absence of LVSD, as does the ejection fraction. Figure 1 also reveals that EMAT is higher in patients with atrial fibrillation compared to those in sinus rhythm both with and without LVSD suggesting that atrial fibrillation alone impairs LV contractility. The ROC curves in Figure 2 reveal that EMAT and SDI are similar in performance for the groups with and without atrial fibrillation.

Table 2 shows sensitivities, specificities and the likelihood ratios for EMAT, SDI, and EF at common thresholds to detect LV systolic dysfunction in groups with and without atrial fibrillation. Note the similar performances for EMAT and SDI independent of the presence of atrial fibrillation. Specificities were high for all populations for EMAT and SDI, with moderate sensitivities (ranging from 30 to 64).

TABLE 1: Demographic and clinical characteristics.

Parameter	No Afib, No LVSD (N = 52)	No Afib, LVSD (N = 103)	Afib, No LVSD (N = 17)	Afib, LVSD (N = 22)
Age (years)	63.8 ± 11.6, 27 – 81	62.0 ± 12.0, 22 – 86	66.7 ± 11.2, 43 – 85	67.7 ± 10.4, 43 – 85*
Male (%)	63%	67%	82%	82%
Height (cm)	170 ± 10, 141 – 190	169 ± 9.1, 149 – 196	173 ± 11, 152 – 192	172 ± 10.6, 150 – 190
Weight (kg)	80.1 ± 19.4, 52 – 148	78.9 ± 15.0, 51 – 117	91.4 ± 24.4, 49 – 160	86.5 ± 22.0, 53 – 132
Heart rate (bpm)	75.3 ± 16.0, 42 – 129	74.5 ± 14.9, 43 – 142	99.0 ± 28.6, 56 – 149*	90.7 ± 14.8, 68 – 119*
QRS duration (ms)	96.4 ± 16.1, 59 – 143	121 ± 36.1, 68 – 235^	90.2 ± 9.8, 74 – 102	110 ± 26.1, 81 – 171^
QTc interval (ms)	418 ± 28.7, 319 – 465	430 ± 32.8, 372 – 528^	407 ± 29.1, 374 – 466	404 ± 33.4, 321 – 483*
EMAT (ms)	83.7 ± 16.5, 58 – 164	100 ± 19.7, 60 – 164^	101 ± 16.8, 79 – 147*	116 ± 20.5, 88 – 164^*
SDI	3.2 ± 1.6, 0.8 – 7.4	4.9 ± 2.6, 0.7 – 10^	3.8 ± 0.7, 2.7 – 4.6	6.0 ± 2.1, 2.9 – 10^
LV EDP (mmHg)	19.9 ± 6.5, 4 – 37	18.6 ± 7.6, 4 – 39	16.4 ± 7.4, 5 – 27	15.1 ± 6.6, 8 – 37*
LV max (dP/dt) (mmHg/s)	2039 ± 301, 1608 – 2928	1189 ± 238, 480 – 1584^	2090 ± 342, 1632 – 2832	1201 ± 254, 648 – 1584^
LV ejection fraction (%)	62.3 ± 14.0, 19 – 83	43.4 ± 18.3, 8 – 84^	57.1 ± 21.1, 10 – 86	40.7 ± 19.2, 15 – 81^
EDV (ml)	116 ± 35.3, 51 – 206	155 ± 63.4, 47 – 337^	107 ± 32.5, 50 – 146	144 ± 59.7, 25 – 264^
ESV (ml)	51.1 ± 24.3, 18 – 135	96.0 ± 56.8, 19 – 261^	49.9 ± 29.5, 19 – 113	97.5 ± 59.7, 40 – 186^

Afib: atrial fibrillation; LV EDP: left ventricular end-diastolic pressure; EDV: end-diastolic volume; EMAT: electromechanical activation time; ESV: end-systolic volume; LVSD: left ventricular systolic dysfunction, defined as LV max(dP/dt) < 1600 mmHg/s; SDI: systolic dysfunction index.

^{*}P < .05 compared across LV systolic dysfunction groups; [†]P < .05. No Afib compared to Afib within the same LV systolic dysfunction group.

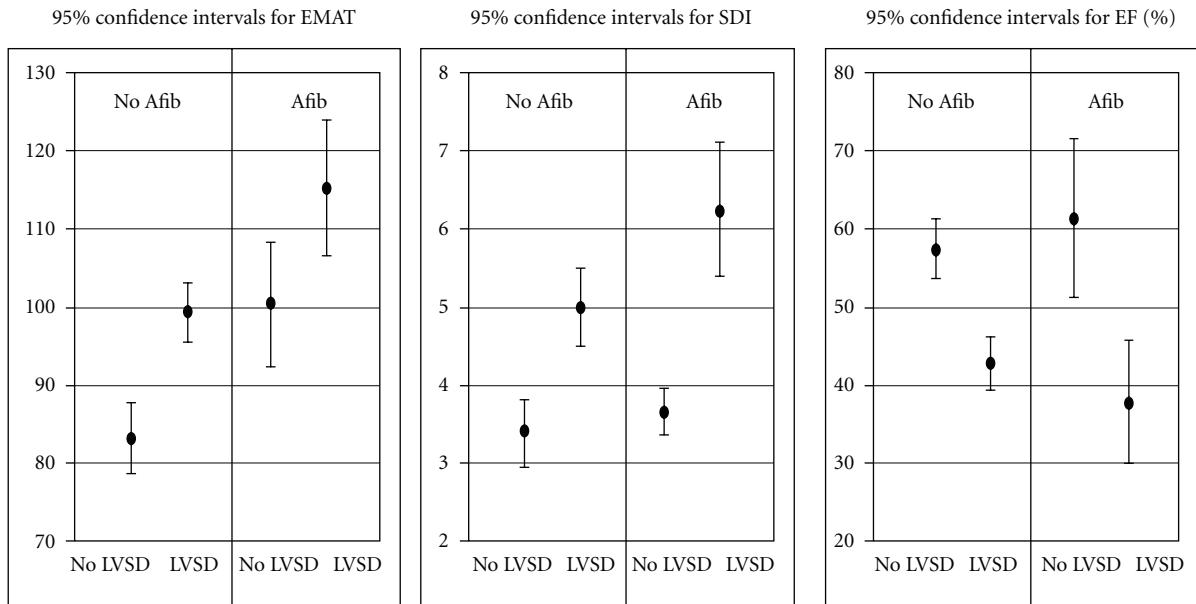


FIGURE 1: The means and 95% confidence intervals for electromechanical activation time (EMAT), the systolic dysfunction index (SDI) and ejection fraction (EF) for populations with and without left ventricular systolic dysfunction (LVSD). Afib: atrial fibrillation; EMAT: electromechanical activation time, msec; SDI: systolic dysfunction index; EF: ejection fraction, %; LVSD: left ventricular systolic dysfunction, defined as LV max(dP/dt) < 1600 mmHg/s.

Ejection fraction had reduced specificities at similar sensitivities to the acoustic cardiographic parameters.

4. Discussion

Noninvasive methods are often employed to identify patients with LVSD. Echocardiography measures several systolic parameters but the beat-to-beat variations in preload with atrial fibrillation make accuracy difficult. A study by Gosselink [17] found that varying left ventricular performance

during atrial fibrillation is determined by cycle length-dependent contractile mechanisms including postextrasystolic potentiation and mechanical restitution, but that beat-to-beat changes in preload consistent with the Starling mechanism are diminished after long and short preceding intervals. Another study using simultaneous biplane views of the left ventricle concludes that systolic function can be accurately assessed in atrial fibrillation by averaging 2 beats with equal subsequent cycle lengths greater than 500 ms [18]. Dubrey [19] found that in atrial fibrillation the average

TABLE 2: Performances of EMAT, SDI, and EF to detect LVSD.

Parameter	Group	% Sensitivity	% Specificity	Pos LR	Neg LR
EMAT@110	No Afib	30	96	7.8	1.4
	Afib	64	82	3.6	2.3
SDI@5.0	No Afib	40	90	4.0	1.5
	Afib	59	100	59	2.4
EF@35%	No Afib	30	96	7.8	1.4
	Afib	45	82	2.6	1.5
EF@50%	No Afib	69	81	3.6	2.6
	Afib	64	76	2.7	2.1

EMAT: electromechanical activation time, msec; SDI: systolic dysfunction index; EF: ejection fraction, %; LVSD: left ventricular systolic dysfunction, defined as $LV \max(dP/dt) < 1600 \text{ mmHg/s}$; Afib: atrial fibrillation, Pos LR: positive likelihood ratio, Neg LR: negative likelihood ratio.

number of beats required to determine cardiac output using Doppler measurements was approximately 13 beats (ranging 4 to 17 beats) or three times that required in sinus rhythm. Therefore, the time required and skill necessary to perform echocardiographic examinations in patients with atrial fibrillation are quite high.

Cardiac magnetic resonance imaging (CMRI) has superior interobserver and intraobserver variability than echocardiography and is the preferred technique by some clinicians for volume and ejection fraction estimation in heart failure patients due to its three-dimensional technique for nonsymmetric ventricles and excellent image quality [20]. But recent literature is mixed on its routine use in the management of atrial fibrillation for evaluation of systolic function. In a recent review of cardiovascular imaging in atrial fibrillation, Wazni et al. recommend the use of CMRI for precise visualization of left atrial and pulmonary vein anatomy [21] but recommend echocardiography for clinical management.

The acoustic cardiography method is a rapid and inexpensive test and does not have the above limitations inherent in echocardiography or cardiac magnetic resonance imaging. The procedure needed to obtain EMAT and SDI requires no more time, effort, or technical skill than that needed for recording a standard 12-lead ECG, and the analysis of the data is fully automated [22]. The parameters are reproducible and represent an average over the 10-second recording. This averaging of values over multiple cardiac cycles improves their performance by minimizing the effect of varying preceding RR intervals as demonstrated for systolic time intervals over 30 years ago [23, 24].

In the present paper, we defined left ventricular systolic dysfunction as $LV \max(dP/dt) < 1600$, a threshold value similar to that used by other investigators [13–15]. Left-ventricular maximum dP/dt is sensitive to changes in contractility and is affected to a lesser extent by both preload and afterload [25, 26]. Left ventricular $\max(dP/dt)$ may be delayed and may follow the opening of the aortic valve in patients with severe LVSD or with marked vasodilatation with very low aortic diastolic pressures. Its sensitivity to preload is greater in ventricles with enhanced contractility, but is reduced in LVSD [27]. Nevertheless, reduced LV

$\max(dP/dt)$ is clinically important because of its association with a poor prognosis [28–30].

EMAT also reflects the rate of left ventricular pressure development since it measures the time required to close the mitral valve. EMAT is similar to $LV \max(dP/dt)$ in that it is influenced by preload via the Starling mechanism invoked by left-ventricular filling pressure. However, EMAT is not affected by afterload resulting from changing systemic vascular resistance or aortic valvular obstruction. In this way, EMAT can be a robust measurement in atrial fibrillation even with other concurrent disease conditions. The systolic dysfunction index combines EMAT with QRS duration, the QR interval, and the strength of the third heart sound. It was developed to provide good detection of systolic dysfunction at values above 5.0, and above 7.5 detects systolic dysfunction with elevated filling pressures [31]. As a continuous variable SDI can provide a means to track changes in systolic function and filling pressures.

Diminished $LV \max(dP/dt)$ is a well-established and accurate marker of LV systolic dysfunction. The present study has shown that acoustic cardiographic parameters discriminate well between normal versus low values of $LV \max(dP/dt)$ in patients with atrial fibrillation. However, it would be useful to know if these parameters also identify patients who are at increased risk of adverse clinical outcomes. Nonacute heart failure patients ($n = 128$) were studied using acoustic cardiography and echocardiography (personal communication, M. Zuber). They were followed for 27.1 ± 14.8 months and all heart failure events and all-cause deaths were recorded (24 events total). Echocardiographic and acoustic cardiographic measurements were evaluated for sensitivity at 90% specificity and the corresponding odds ratios. Echocardiographic parameters had lower sensitivity (T deceleration time 26% at 180 ms; EF 17% at 45%; E/E' ratio 18% at 15; E/A 25% at 1.8) than the acoustic cardiographic parameters (EMAT 38% at 120 ms; SDI 45% at 5.0). The echocardiographic measurements also had lower odds ratios (ranging from 0.4 for T deceleration time to 2.2 for E/E' ratio) than acoustic cardiographic parameters (ranging from 5.9 for EMAT to 7.5 for SDI). This study would indicate that both EMAT and SDI have superior prognostic value over the traditional echocardiographic measurements.

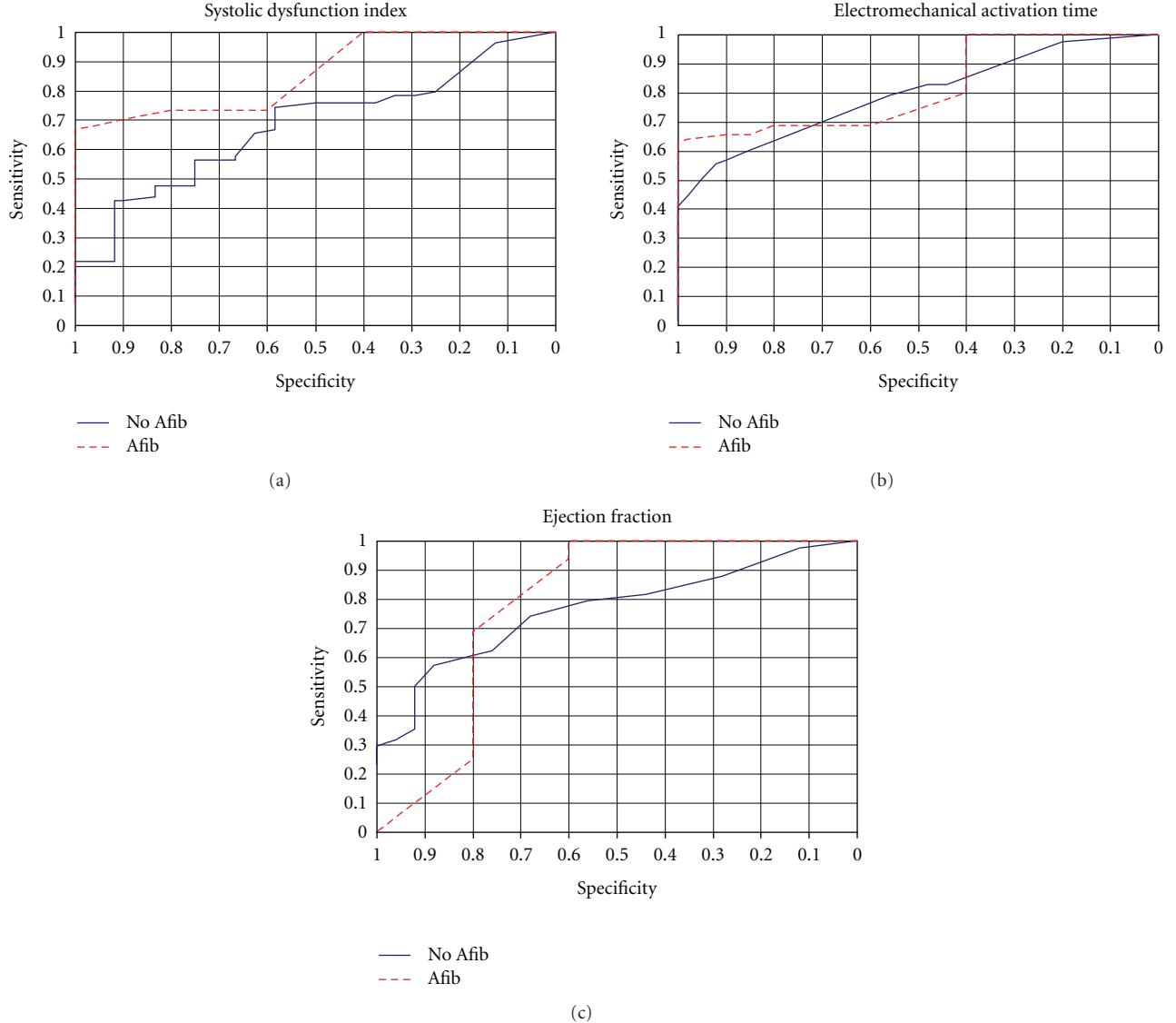


FIGURE 2: Receiver-operating characteristic (ROC) curves are presented for electromechanical activation time, the systolic dysfunction index and ejection fraction for populations with (red curve) and without atrial fibrillation (blue curve). Afib: atrial fibrillation.

In another study of patients hospitalized for acute heart failure ($n = 45$), acoustic cardiographic recordings were taken within 24 hours of admission, before discharge and 2 weeks after discharge [32]. Adverse post-discharge events were cardiac death or rehospitalization for heart failure. Patients were followed for 242 ± 156 days. Predischarge and 2-week postdischarge %EMAT (defined as EMAT divided by the R-R interval) was significantly associated with adverse post-discharge events, with or without adjustment for age, gender, left ventricular EF, E/E' by Doppler echocardiography, and serum N-terminal probrain natriuretic peptide.

We conclude that acoustic cardiography detects left ventricular systolic dysfunction in patients with atrial fibrillation. This is particularly important when repeat assessment is desired and in situations where invasive (cardiac catheterization) or noninvasive (echocardiographic or cardiac magnetic

resonance imaging) assessment of LV function is not feasible or readily available.

5. Limitations of the Study

Although it is similar to older methods used to obtain systolic time intervals, acoustic cardiography is a relatively new method of quantifying cardiac function and has limited routine use. There was not a control group of healthy subjects due to the fact that this was an invasive cardiac catheterization study. Not all the recordings of left ventricular dP/dt were performed with manometer-tipped catheters. Left ventricular ejection fraction was calculated using monoplane ventriculography. Although short-acting diuretics were withheld on the morning of the catheterization, the subjects varied with respect to the types and

dosages of other cardiac drugs that they were receiving. Since beta adrenergic blockers, vasodilators, ACE inhibitors and other cardiac drugs influence ventricular performance, this pharmacological variability may have affected our results.

Conflict of Interests

Dr. P. Arand is an employee of Inovise Medical, Inc. The remaining authors have no conflict of interests and will have no financial gain from the writing or the publication of this paper.

Acknowledgment

The authors thankfully acknowledge the assistance of Dr. Peter Bauer, Inovise Medical, Inc., Beaverton, OR for data analysis support.

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