

## Importance of Atrial Systole to Ventricular Filling Predicted by Transesophageal Echocardiography

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This study documented mitral flow velocity patterns in anesthetized patients with ischemic heart disease and left ventricular dysfunction and investigated the relationship between transmitral flow velocity measurements and the hemodynamic response to ventricular pacing. Twenty-four patients in sinus rhythm without evidence of mitral valve disease undergoing elective myocardial revascularization were studied. Anesthesia consisted of a high-dose opioid-muscle relaxant-oxygen technique. After endotracheal intubation a 3.5-MHz phased-array transesophageal echocardiographic probe was inserted and positioned to obtain a long-axis view of the left atrium and left ventricle. The Doppler sample volume was placed at the mitral annulus with minimal cursor angulation, and the biphasic velocity tracing of transmitral blood flow was recorded. A hemodynamic profile was obtained, and cardiac output was measured in triplicate by thermodilution. Ventricular pacing was then instituted and the hemodynamic and thermodilution measurements were repeated. The peak early filling (E) velocity was  $0.34 \pm 0.11$  m/s, and the peak atrial (A) velocity was  $0.38 \pm 0.09$  m/s. The mean E:A ratio was  $0.91 \pm 0.3$ , and the median value was 0.88. In sinus rhythm the cardiac index of those patients with an E:A > 0.88 (group 1) was  $1.97 \pm 0.32$  l/min and those with an E:A < 0.88 (group 2) was  $1.76 \pm 0.50$  (NS). During ventricular pacing the patients in group 1 ( $1.56 \pm 0.32$  l/min) had significantly higher cardiac indices than those in group 2 ( $1.21 \pm 0.31$  l/min) ( $P < 0.02$ ). It is concluded that peak E velocities and E:A ratios are markedly lower in anesthetized patients with ischemic heart disease whose lungs are mechanically ventilated than in awake normals and that patients with E:A ratios < 0.88 had more marked decreases in cardiac index and stroke index with the loss of atrial contraction during ventricular pacing. (Key words: Measurement technique: transesophageal echocardiography. Heart: atrial systole; ventricular pacing. Pulsed-wave Doppler: transmitral blood flow.)

TRANSESOPHAGEAL ECHOCARDIOGRAPHY (TEE) was initially used to diagnose myocardial ischemia<sup>1</sup> and assess left ventricular dimensions and ejection.<sup>2</sup> Some trans-

esophageal systems have the capacity to perform pulsed-wave Doppler echocardiographic measurements, which permit determination of blood flow velocity in a specified location over time. Blood flow velocities sampled at the level of the mitral valve can be used to calculate stroke volume and cardiac output<sup>3</sup> and evaluate the filling pattern of the left ventricle.<sup>4</sup>

Ventricular filling is biphasic and consists of an early rapid filling phase and an atrial contraction phase.<sup>5</sup> Normally, 85–90% of filling occurs during the early rapid phase, and the remainder follows atrial systole.<sup>6</sup> In some pathologic conditions, such as aortic stenosis and hypertrophic cardiomyopathy, ventricular filling is more dependent on atrial contraction, and the loss of atrial systole may result in hemodynamic deterioration.<sup>7</sup> Because various anesthetic agents and interventions are associated with the loss of atrial contraction, a means to quantitate the relative contribution of the atrial contraction to global ventricular filling is desirable. This information could be valuable in the planning of anesthetic or pacing techniques because it could help predict and avoid hemodynamic deterioration. This is the first study using transesophageal pulsed-wave Doppler echocardiography to document transmitral blood flow velocities in anesthetized patients with severe ischemic heart disease. It also investigated the relationship between transmitral blood flow velocity and the hemodynamic response to ventricular pacing.

### Methods

The study protocol was approved by the institutional research administrative committee, and informed written consent was obtained from each patient. Twenty-four ASA Physical Status 3 or 4 patients in sinus rhythm, without evidence of mitral valve dysfunction, and scheduled for elective myocardial revascularization surgery were studied. The absence of mitral regurgitation was documented by physical examination, preoperative echocardiogram, contrast left ventriculogram, and intraoperative pulsed-wave Doppler mapping of the transmitral flow. Left ventricular function ranged from "normal" to "moderately depressed." The patients ranged in age from 37 to 76 yr with a mean age of 62 yr. Patients with esophageal disease, unstable hemodynamics, or acute evolving myocardial ischemia were excluded from the study.

Ninety minutes prior to the anesthetic induction the patients received morphine (0.1–0.15 mg/kg im) and scopolamine (0.003–0.006 mg/kg im). Calcium channel-

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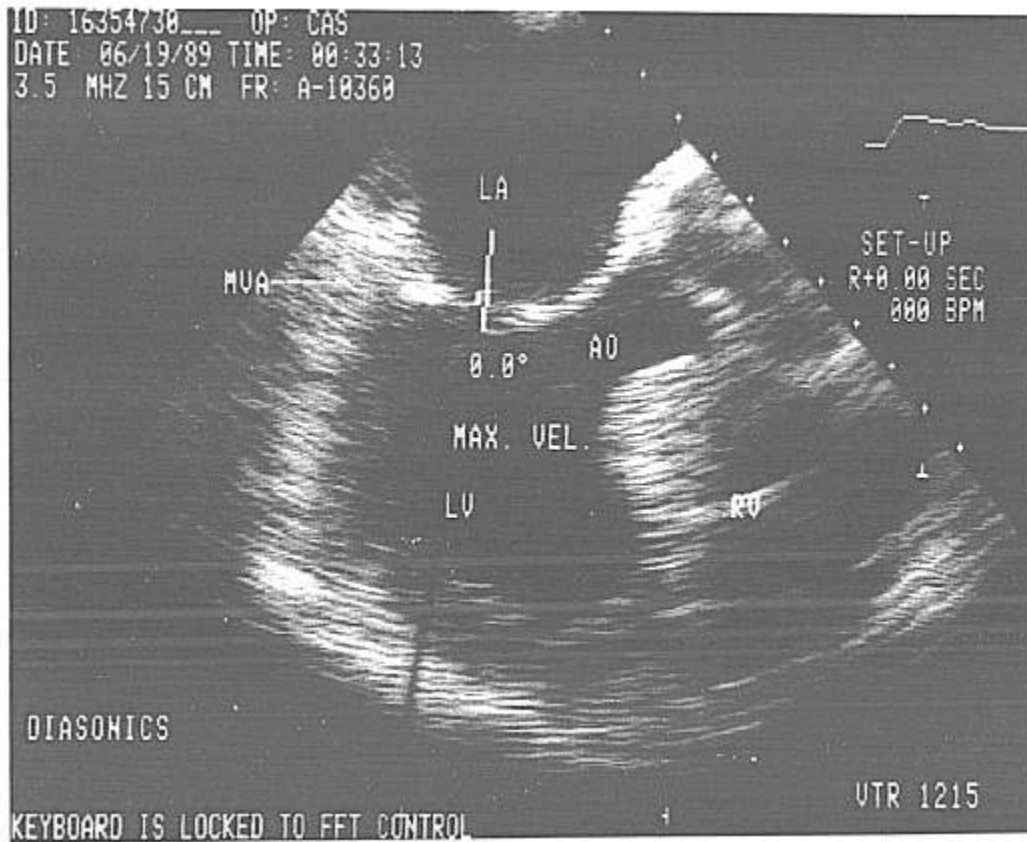


FIG. 1. Transesophageal echocardiographic long-axis view of the left atrium (LA), mitral valve annulus (MVA), and left ventricle (LV). The aortic outflow tract (AO) and the right ventricle (RV) are also shown.

blocking drugs,  $\beta$ -adrenergic-blocking drugs, and nitrates were continued up to the time of surgery. Upon arrival in the operating room, peripheral venous, radial arterial, and 7.5-Fr pulmonary arterial (American Edwards Laboratories, Santa Ana, California) catheters were inserted using local anesthesia. Electrocardiographic leads II and modified  $V_5$ , oxygen saturation, and respiratory gas concentrations were also monitored. Electrocardiographic and pressure tracings were recorded on a Hewlett-Packard Series 78000 Multichannel Pressure Recorder (Hewlett-Packard, Waltham, Massachusetts) from equisensitive Spectromed P2310 Pressure Transducers (Spectromed, Woodbridge, New Jersey) calibrated by aneroid manometry. Before each set of measurements, the zero reference point of the transducers was positioned at the level of the right atrium, 5 cm posterior to the sternal angle of Louis. Intravenous fluid administration was limited to 500 ml of crystalloid.

Hemodynamic measurements consisted of heart rate (HR), mean arterial pressure (MAP), systolic pulmonary artery pressure (PAS), diastolic pulmonary artery pressure (PAD), central venous pressure (CVP), and cardiac output (CO). Thermodilution data were collected using the pul-

monary arterial catheter and a 9520-A Cardiac Output Computer (American Edwards Laboratories, Santa Ana, California). Ten-milliliter boluses of 5% dextrose were injected until three values within 10% of one another were obtained. Stroke volume (SV), stroke index (SI), and cardiac index (CI) were also computed using standard formulas.

Fentanyl (100  $\mu$ g/kg) and diazepam (0.1–0.3 mg/kg) were used to induce anesthesia while muscle relaxation was obtained with pancuronium (0.1 mg/kg). Following endotracheal intubation the patients' lungs were mechanically ventilated to maintain normocarbida, and a 3.5 MHz phased-array transesophageal echocardiographic probe (Diasonics, Milpitas, California) was introduced into the patient's esophagus. The probe was connected to a Diasonics 6400 ultrasonograph and positioned to obtain a long-axis view of the left atrium and ventricle. Following pericardiotomy a 0.25-cm Doppler sample volume was placed at the level of the mitral annulus, with the transducer oriented to optimally align the cursor with the axis of blood flow (fig. 1). A spectral display of the transmitral blood flow velocity was recorded on photographic paper for later analysis (fig. 2). Baseline hemodynamic and ther-

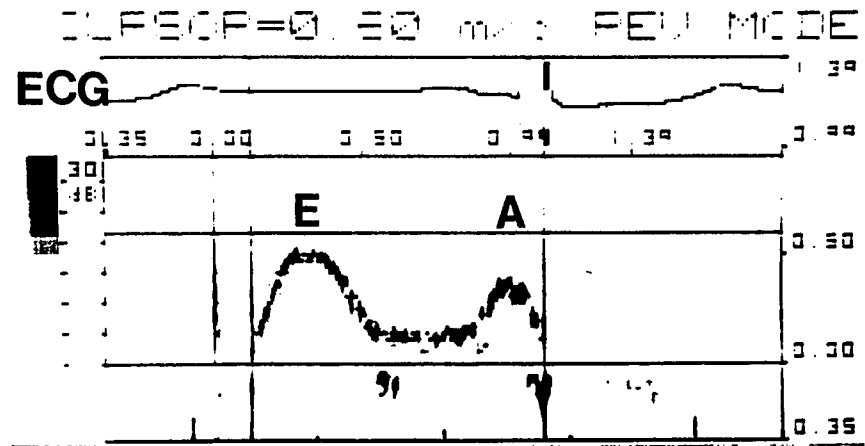


FIG. 2. Recording of the pulse wave Doppler transmitral blood flow velocities. Two wave components are seen: the peak early (E) phase and the peak atrial (A) phase.

modulation measurements in the presence of sinus rhythm (SR) were then obtained during brief periods of apnea at end-expiration. At this point, alligator clip electrodes were applied to the right ventricular epicardium and the sternal retractor, and asynchronous unipolar ventricular pacing was instituted at the lowest rate that ensured complete ventricular capture. Following a 1-min period of ventricular pacing (VP), the full set of hemodynamic and thermomodulation measurements were repeated at end-expiration during brief periods of apnea.

The Doppler recordings were analyzed on a Dextra D-200 Advanced Cardiac Analysis System (Dextra Medical Inc, Long Beach, California). After recalibrating for each patient, the transmitral flow pattern was traced using a digitizing tablet. The system then analyzed the image and performed the following measurements: peak early filling velocity (E), peak atrial filling velocity (A), and the ratio of E:A. Based on the results of these measurements, the patients were divided into two groups. Those with an E:A above the median (0.88) were placed in group 1 (n = 12) and those patients with an E:A below the median were placed in group 2 (n = 12). The groups were not significantly different in age, LV function, medications, or number of diseased vessels. Intragroup comparisons were made using a paired Student's *t* test to examine the effect of changing from SR to VP. Intergroup comparisons were made in SR and during VP using an unpaired Student's *t* test to examine the influence of E:A. Bonferroni's modification was applied to correct for multiple *t* tests. Significance was defined as  $P < 0.05$ . All data are reported as mean  $\pm$  SD.

## Results

### MEASUREMENTS DURING SINUS RHYTHM

As a group, the 24 patients had a peak early velocity (E) of  $0.34 \pm 0.11$  m/s, a peak atrial velocity (A) of  $0.38$

$\pm 0.09$  m/s, and an E:A ratio of  $0.91 \pm 0.3$ . During sinus rhythm CI was  $1.87 \pm 0.41$   $l \cdot \text{min}^{-1} \cdot \text{m}^{-2}$  and SI was  $34 \pm 7$   $\text{ml}/\text{m}^2$  (table 1).

The patients in group 1 had the following transmitral flow velocity characteristics: E =  $0.41 \pm 0.08$  m/s, A =  $0.37 \pm 0.09$  m/s, and E:A =  $1.15 \pm 0.21$ . Hemodynamic measurements were as follows: HR =  $54 \pm 8$  beats per min, CI =  $1.97 \pm 0.32$   $l \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ , and SI =  $37 \pm 7$   $\text{ml}/\text{m}^2$  (table 2).

Analysis of the transmitral flow velocity profiles of the patients in group 2 during sinus rhythm revealed the following results: E =  $0.26 \pm 0.07$  m/s, A =  $0.39 \pm 0.09$  m/s, and E:A =  $0.67 \pm 0.13$ . During SR the hemodynamic measurements of the patients in group 2 were not significantly different from those in group 1: HR =  $58 \pm 8$  beats per min, CI =  $1.76 \pm 0.5$   $l \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ , and SI =  $31 \pm 7$   $\text{ml}/\text{m}^2$  (table 2).

### MEASUREMENTS DURING VENTRICULAR PACING

The 24 patients had a lower CI ( $1.38 \pm 0.35$   $l \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ ), and SI ( $22$   $\text{ml}/\text{m}^2$ ) with asynchronous pacing (table 1). Intragroup analysis (paired *t* test) revealed

TABLE 1. Hemodynamics for the Total Study Population (n = 24)

	SR	VP
HR (beats/min)	$56 \pm 8$	$65 \pm 9^*$
MAP (mmHg)	$74 \pm 8$	$61 \pm 9^*$
PAD (mmHg)	$11 \pm 4$	$11 \pm 5$
CI ( $l \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ )	$1.87 \pm 0.41$	$1.38 \pm 0.35^*$
SI ( $\text{ml}/\text{m}^2$ )	$34 \pm 7$	$22 \pm 6^*$
E (M/s)	$0.34 \pm 0.10$	—
A (M/s)	$0.38 \pm 0.09$	—
E:A	$0.91 \pm 0.29$	—

SR = sinus rhythm; VP = ventricular pacing; HR = heart rate; MAP = mean arterial pressure; PAD = pulmonary artery diastolic pressure; CI = cardiac index; SI = stroke index; E = peak early velocity; A = peak atrial velocity; E:A = ratio of peak early to peak atrial velocity.  
\*  $P < 0.05$ .

TABLE 2. Hemodynamics for Groups 1 and 2

	Group I E:A > 0.88 (n = 12)		Group II E:A < 0.88 (n = 12)	
	SR	VP	SR	VP
HR (beats/min)	55 ± 9	65 ± 8*	58 ± 8	65 ± 10†
MAP (mmHg)	75 ± 10	61 ± 8†	74 ± 10	62 ± 10*
PAD (mmHg)	11 ± 3	12 ± 5	11 ± 4	11 ± 5
CI (l · min <sup>-1</sup> · m <sup>-2</sup> )	1.97 ± 0.32	1.56 ± 0.32*	1.76 ± 0.5	1.21 ± 0.31*†‡
SI (ml/m <sup>2</sup> )	37 ± 7	24 ± 6*	31 ± 7	19 ± 4*§
E (m/s)	0.41 ± 0.08	—	0.26 ± 0.07	—
A (m/s)	0.37 ± 0.09	—	0.39 ± 0.09	—
E:A	1.15 ± 0.21	—	0.67 ± 0.13	—

Intragroup comparisons (paired *t* test): \**P* < 0.001; †*P* < 0.005.  
Intergroup comparisons (unpaired *t* test): ‡*P* < 0.02; §*P* < 0.01.

significant (*P* < 0.001) decreases in CI and SI and a small increase in HR (*P* < 0.05) in both groups 1 and 2 with asynchronous VP.

Intergroup comparisons (unpaired *t* tests) during VP showed several significant differences. CI (*P* < 0.04) and SI (*P* < 0.02) were significantly lower in group 2 than group 1 during VP. Intergroup comparisons showed no significant differences during sinus rhythm and VP in HR, PAD, and MAP. All 24 patients completed the study, and there were no complications attributable to the investigation. Furthermore, the E:A ratio weakly correlated with the percent change in SI in an inverse fashion (*r* = -0.44, *P* < 0.05) (fig. 3).

Discussion

The current investigation examined diastolic transmitral flow patterns and the hemodynamic response to ventricular pacing in 24 patients with coronary artery disease. Those patients with early diastolic to atrial (E:A) peak velocity ratios below the median value had lower

cardiac indices and stroke indices during asynchronous ventricular pacing than their counterparts with higher (E:A) ratios.

In patients with a normal cardiovascular system, loss of atrial contraction results in minimal changes in CI, SI, and MAP. However, in patients with cardiovascular disease, loss of atrial contraction may significantly reduce MAP, CI, and SI.<sup>7</sup> One attempt to define the importance of atrial systole investigated the relationship between pulmonary capillary wedge pressure and the atrial contribution to ventricular filling and found a weak negative correlation (*r* = -0.53).<sup>8</sup>

METHODOLOGIC CONSIDERATIONS

Pulsed-wave Doppler echocardiography of transmitral blood flow provides a noninvasive method of examining left ventricular filling. This technique yields a recording of blood velocity over time through the mitral valve. In patients with synchronized atrial/ventricular contraction, the normal filling pattern is displayed as a biphasic tracing

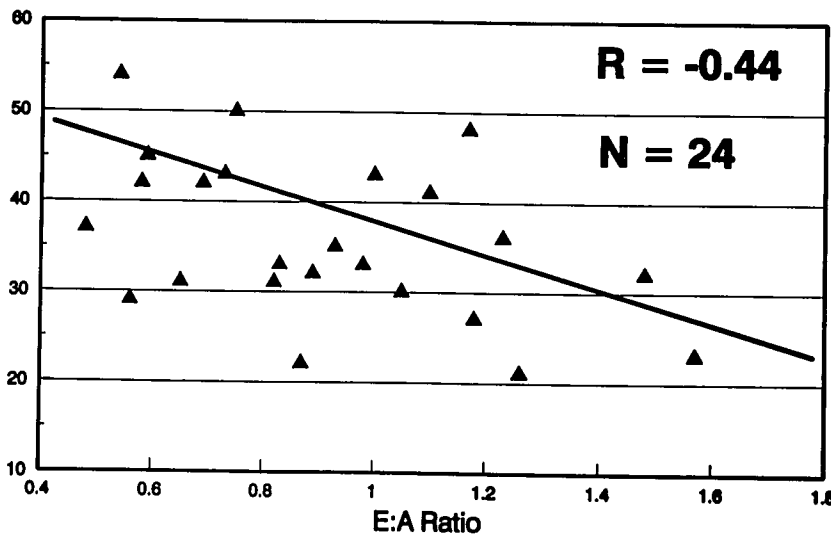


FIG. 3. Decrease in stroke index versus E:A ratio.

depicting a rapid early filling phase (E) followed by diastasis and completed with atrial contraction (A). In addition to peak velocity measurements, another easily calculated parameter is the ratio of the peak velocities (E:A). These measurements can be performed at the level of the mitral annulus or at the level of the valve leaflet tips. The velocities will be higher at the tips by a ratio of 1.3:1.<sup>9</sup> This study measured the velocities at the annular level. Thus, the values reported in this study are lower than the values in studies in which the measurements were performed at the tips of the valve leaflets.

Doppler measurements of E and A filling velocities have been shown to correlate closely with values obtained by angiographic techniques.<sup>10</sup> Based on the concept that peak early diastolic and atrial velocities reflect the relative contribution of ventricular filling during their respective phases of diastole, this study examined the relationship between E:A and the hemodynamic response to loss of atrial contraction by asynchronous ventricular pacing. In the current study of a group of patients with multivessel coronary artery disease, it was shown that these patients were significantly dependent on atrial contraction. Furthermore, despite similar loading conditions and heart rate, in patients with E:A ratios below the median value, the hemodynamic response to ventricular pacing was more pronounced.

#### ALTERNATIVE EXPLANATIONS

Hemodynamic and thermodilution measurements were obtained during sinus rhythm and ventricular pacing. Physiologically, ventricular pacing differs from sinus rhythm in two ways: 1) atrial contraction is lost, and 2) the pattern of depolarization is abnormal. Thus, the differences observed may not have been only from the loss of atrial contraction. However, previous work "has demonstrated that the absence of synchronized atrioventricular activity rather than aberrant ventricular depolarization is primarily responsible for the hemodynamic difference" observed.<sup>11</sup> Further confirmation that the main effect of ventricular pacing is the elimination of atrial systole was provided by Kuo *et al.*<sup>6</sup> Using transmitral pulsed-wave Doppler echocardiography, they demonstrated that the time-velocity integral of the passive filling phase of diastole during sinus rhythm correlated closely ( $r = 0.983$ ,  $y = 1.01x - 0.16$ ) with the time-velocity integral during ventricular pacing. These two studies support the assumption that the predominant effect of VP is the loss of atrial contraction.

Another potentially confounding variable is that the ventricular pacing may have produced myocardial ischemia, and the observed decreases in CI and SI may have been from acute ventricular dysfunction. Because the baseline heart rates were slow, the minimal increases ( $56 \pm 8$  to  $65 \pm 9$  beats per min) during VP resulted in low

normal rates, which were unlikely to cause ischemia. Furthermore, there was no electrocardiographic evidence of ischemia during the study. Thus, the decreases in CI and SI that occurred during VP were not likely due to abnormal contractile patterns or ischemia-induced systolic dysfunction but were due to altered ventricular diastolic filling.

#### RELATIONSHIP OF THE CURRENT STUDY TO PREVIOUS STUDIES

The E:A ratio that was used as the dividing point between groups 1 and 2 in this study (0.88) is an abnormally low value compared with a normal population. However, this dividing point is consistent with the work of Fujii *et al.*,<sup>4</sup> who showed that patients without cardiovascular disease had an average E:A ratio of 2.27 and patients with multivessel coronary artery disease had an average E:A of 0.82. Another factor that distinguishes the sample population in the current study is that our patients were anesthetized and their lungs were mechanically ventilated.

This study has demonstrated that in anesthetized patients with ischemic heart disease atrial contraction plays an important role in ventricular filling. In addition, transmitral blood flow velocity profiles determined by transesophageal pulsed-wave Doppler echocardiography can be used to assess the contribution of atrial systole to cardiac output. These results are consistent with those of Pearson *et al.*,<sup>12</sup> who showed that in awake patients the percent increase in cardiac output obtained by optimization of atrial contraction weakly but significantly correlated with Doppler-derived E:A in an inverse fashion.

#### LIMITATIONS

In applying these conclusions there are two important factors to consider. First, although the E:A ratio is an easily measured parameter of transmitral blood flow, it is by no means constant in a given patient. These filling velocities are affected by a multitude of factors, including the following: 1) left atrial compliance; 2) left atrial contractile state; 3) pulmonary venous return;<sup>13</sup> 4) mitral valve function; 5) myocardial relaxation;<sup>14</sup> 6) left ventricular chamber stiffness;<sup>15</sup> 7) external constraints (*i.e.*, the pericardium); and 8) the phase of the respiratory cycle. Thus, for the assessment of atrial contraction to be valid, the determination should be made frequently and as close to the proposed intervention as possible. Second, patients in this study were separated into two groups with a dividing point of  $E:A = 0.88$ . E:A values less than this level represent a severely abnormal state, and the results are only applicable to patients with severe cardiovascular disease. Because these are also the patients most likely to suffer from the loss of atrial contraction, the results of this study are clinically relevant.

We have shown that patients with multivessel coronary artery disease under general anesthesia had markedly abnormal transmitral flow velocities with the major reduction occurring in the early rapid filling phase of diastole (normal peak E = 0.9 m/s, observed peak E = 0.4 m/s). Those patients with E:A ratios < 0.88 experienced a more marked reduction in cardiac and stroke indices during the loss of atrial contraction. An important area for further investigation is the identification of treatable conditions that alter the dependence of ventricular filling upon atrial systole and the use of transmitral flow velocity profiles to track therapeutic efforts.

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