“Stunning” of the Left Atrium After Spontaneous Conversion of Atrial Fibrillation to Sinus Rhythm

Demonstration by Transesophageal Doppler Techniques in a Canine Model

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Objectives. This study compared left atrial and left atrial appendage contraction velocities in sinus rhythm before and after a brief period of atrial fibrillation in a canine model.

Background. In patients, left atrial appendage contraction velocities measured during sinus rhythm after cardioversion from atrial fibrillation are depressed relative to left atrial appendage emptying velocities measured during atrial fibrillation, suggesting that the left atrial appendage is mechanically “stunned.”

Methods. This phenomenon was studied in a canine model of acute (60 min) pacing-induced atrial fibrillation followed by spontaneous reversion to sinus rhythm using epicardial and transesophageal pulsed wave Doppler. Unique features of the model include: 1) comparison of left atrial function postconversion to baseline sinus rhythm rather than to measurements during atrial fibrillation, 2) control of the duration of atrial fibrillation and 3) elimination of the extraneous influences of direct current shock and antiarrhythmic agents, which may independently depress left atrial function.

Results. Hemodynamic conditions (heart rate, mean arterial pressure, cardiac output, mean pulmonary artery pressure, mean right atrial pressure and mean left atrial pressure) at baseline, during 60 min of atrial fibrillation and after reversion to sinus rhythm were constant throughout the study period. Peak left atrial contraction velocities (measured from the transmitral flow velocity profile) were significantly (p < 0.02) reduced to 64 ± 22% of baseline values upon spontaneous conversion of atrial fibrillation to sinus rhythm and recovered to basal values by 20 min after resumption of sinus rhythm. Peak left atrial appendage contraction velocities were significantly (p < 0.001) reduced to 49 ± 24% of baseline values upon spontaneous conversion of atrial fibrillation to sinus rhythm and recovered to basal values by 40 min after reversion to sinus rhythm.

Conclusions. Even brief (60 min) periods of atrial fibrillation in normal canine hearts result in marked depression of global left atrial systolic function and regional left atrial (left atrial appendage) systolic function upon resumption of sinus rhythm. This “mechanical stunning” of left atrial systolic function appears to be more profound and of longer duration for the left atrial appendage compared with the left atrium as a whole, which may predispose the appendage to blood stasis and thrombus formation. Chronic models of atrial fibrillation need to be developed to examine the impact of longer periods of atrial fibrillation upon the magnitude and duration of postconversion left atrial “stunning.”

(J Am Coll Cardiol 1998;32:2081–6)
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Despite the prompt resumption of sinus rhythm after cardioversion from atrial fibrillation, mechanical shortening of the left atrial myocardium is often absent or impaired initially. Such left atrial systolic “stunning” has been demonstrated by pulsed Doppler measurements from the transmitral flow velocity profile in patients (1–4) and by direct measurements using paired ultrasonic crystals sutured to the left atrial wall in a porcine model of acute atrial fibrillation (5,6).

Transesophageal echocardiography provides a clinically applicable tool for evaluating left atrial function, identifying thrombus and defining conditions predisposing to thrombus formation during and after atrial fibrillation (7–11). The size of the left atrial appendage and the presence of dense spontaneous echocardiographic contrast within the left atrium are associated with an increased risk for thrombus formation during atrial fibrillation (7,9,10), and the identification of decreased left atrial appendage emptying velocities (<15–25 cm/s) during atrial fibrillation may predict thrombus formation (8,10,11). Transesophageal echocardiographic studies in patients immediately after cardioversion have demonstrated: 1) initial impairment of overall atrial contraction (12), 2) depression of left atrial appendage contraction velocities to values below those...
measured during atrial fibrillation (13) and 3) worsening or de novo development of left atrial spontaneous echocardiographic contrast reflecting stagnant blood flow (12,13). Collectively, these observations suggest that cardioversion to sinus rhythm from atrial fibrillation results in “stunning” of the left atrium. One explanation for the occurrence of thromboembolism after cardioversion in patients free of left atrial thrombi before cardioversion may relate to the predilection for left atrial thrombus formation due to left atrial “stunning” in the postcardioversion recovery period (12).

Transesophageal echocardiographic studies of postcardioversion atrial “stunning” in patients are complicated by several uncontrollable factors that influence the time course of recovery of mechanical function. Longer duration of atrial fibrillation probably prolongs recovery from atrial “stunning” and is a parameter that is difficult to accurately measure in clinical studies (14). The mode of cardioversion, whether spontaneous, pharmacologic or electrical, may influence the duration of postconversion atrial “stunning” (15–17). Finally, in the usual clinical study there is no baseline assessment of left atrial or postconversion atrial “stunning” (15–17). Accordingly, we undertook this study to assess the magnitude of left atrial “stunning” and the time course of its recovery in a canine model of acute (60 min) atrial fibrillation followed by spontaneous reversion to sinus rhythm. In such a model we could examine the effects of a predetermined duration of atrial fibrillation on postconversion left atrial stunning independent of the extraneous influences of therapeutic maneuvers utilized to achieve cardioversion from sinus rhythm.

Methods

Animal preparation. Animal care and experimental conduct conformed to the position of the American Heart Association on research animal use (adopted November 11, 1984) and had the prior approval of the Institutional Review Board and the Animal Care Committee. After an overnight fast, 10 heart worm–free, male mongrel dogs weighing 15–25 kg were sedated with intramuscular xylazine, 1.0 to 2.0 mg/kg. Intravenous alpha-chloralose, 85 mg/kg, was then administered to achieve anesthesia, and supplemental anesthetics were administered during the experiment to maintain a surgical plane of anesthesia. Data were collected only after hemodynamically stable conditions were achieved. After endotracheal intubation, the dogs were ventilated with a volume-cycled respirator (Harvard Apparatus Co., S. Natick, Massachusetts) at a tidal volume of 15 mL/kg adjusted to achieve stable arterial blood gases (oxygen tension 60–100 mm Hg, carbon dioxide tension 30–40 mm Hg, pH 7.35–7.45). The right femoral artery, right femoral vein, right external jugular vein and left external jugular vein were isolated and cannulated. The heart was exposed by median sternotomy and suspended in a pericardial cradle.

Limb lead II of the electrocardiogram was recorded with intramuscular needle electrodes and the signals were routed simultaneously to a multichannel amplifier (2800S; Gould Electronics, Valley View, Ohio). We recorded hemodynamic data at a strip chart speed of 25 mm/s and Doppler spectra (XP-10 echocardiograph; Acuson, Mountain View, California) at a scrolling speed of 50 mm/s. A 7F bipolar (5-mm interelectrode distance) pacing catheter introduced via the left external jugular vein was advanced into the right atrium and positioned so that its four-ring electrodes made stable contact with the right atrial free wall to obtain bipolar recordings of right atrial electrograms. These electrograms were routed both to the multichannel amplifier and the echocardiograph. A fluid-filled angiographic catheter positioned in the descending thoracic aorta from the right femoral artery was used to measure central arterial pressure. A fluid-filled triple lumen thermodilution flotation catheter (Viggo-Spectramed, Oxnard, California) was advanced from the right external jugular vein to the pulmonary artery to measure pulmonary artery pressure and right atrial pressure. Cardiac output was measured in triplicate and averaged with a thermodilution computer (Viggo-Spectramed). A left pulmonary vein was isolated and cannulated with a fluid-filled polyethylene cannula to measure left atrial pressure. All hemodynamic measurements were obtained with equisensitive strain gauges (P23Db; Gould Electronics, Valley View, Ohio) leveled at the midpoint of the anteroposterior diameter of the chest and calibrated with a mercury sphygmomanometer. Bipolar patch electrodes were sutured to the epicardial surfaces of the right atrium and the right ventricle, and positioned to achieve stable capture at low current thresholds (<10 mA, 1-ms pulse width) for both dual-chamber pacing and single-chamber rapid atrial pacing.

A 5-MHz monoplane transesophageal echocardiographic probe was passed into the esophagus and positioned posterior to the left atrium under echocardiographic guidance. The left atrial appendage was imaged adjacent to the circular cross section of the ascending aorta in a transverse short-axis imaging plane through the base of the heart. The pulsed-wave Doppler cursor was then aligned parallel to the long axis of the left atrial appendage and the sample volume positioned 5 mm proximal to the orifice of the left atrial appendage. After a stable quadriphase left atrial appendage flow signal (18–21) was obtained in sinus rhythm, the probe was maintained in a stable orientation with respect to the endocardial boundaries of the left atrial appendage. In addition, the control knobs for antero-posterior and lateral probe tip control were locked and the depth of esophageal intubation by the probe was secured by umbilical ties. A 5-MHz transthoracic echocardiographic probe was positioned gently over the epicardial surface of the left ventricular apex and directed parallel to the left ventricular long axis towards the center of the mitral annular plane. Echocardiographic guidance and manual positioning of the probe were employed to image the heart in an apical four-chamber view transecting the left ventricular apex and the crux of the heart. The pulsed Doppler cursor was aligned parallel to transmitral inflow using color flow Doppler imaging and the imaged mitral valvular structures as guidelines. The sample volume was positioned just distal to the mitral leaflet tips,
where maximal peak velocities of early ventricular diastolic and atrial systolic velocities were recorded as the typical biphasic transmitral inflow velocities in sinus rhythm. Minor adjustments in Doppler cursor positioning were performed to achieve optimal flow signals characterized by: 1) an accompanying pure tone audio signal, 2) a distinct spectral envelope and 3) maximal peak velocities. Attention was directed towards reproducing the epicardial positioning of the probe and the anatomic relation of the Doppler cursor to internal anatomic landmarks on each successive acquisition of transmitral flow velocity data.

**Experimental protocol.** After stable anesthetic conditions were achieved, the right atrium and right ventricle were sequentially paced at cycle lengths 100 ms shorter than the intrinsic sinus cycle length (range 450–990 ms, mean 724 ± 158 ms) and atrioventricular intervals ranging from 100 to 150 ms (mean 123 ± 22 ms). These intervals were selected to overdrive the underlying sinus rhythm and ensure capture of both the atria and ventricles. Once stable hemodynamic conditions were achieved, baseline measurements of hemodynamics, transesophageal pulsed Doppler recordings of left atrial appendage contraction velocities and epicardial pulsed Doppler recordings of transmitral flow velocities were obtained.

Atrial fibrillation was then induced by rapid atrial pacing (constant current stimulator with square wave output of 2–10 mA and 1-ms pulse width) at an interstimulus interval of 100–200 ms. Atrial fibrillation was confirmed during 30-s periods of interruption of rapid atrial pacing by the following observations: 1) continuous fractionated potentials recorded on the atrial electrogram from the bipolar electrode catheter, 2) pulsed Doppler recordings of chaotic left atrial appendage contraction velocities demonstrating irregular cycle length (<150 ms) and widely varying amplitudes, typical of waveforms seen in patients with atrial fibrillation (8–11,18,22) and 3) surface electrocardiogram revealing an irregularly irregular ventricular response (88 ± 52 beats/min).

Pilot studies were performed to determine the impact of duration of pacing-induced atrial fibrillation upon left atrial appendage contraction velocities after resumption of atrial fibrillation to sinus rhythm. Pacing-induced atrial fibrillation for periods of 10–20 min resulted in no systematic depression (relative to baseline measurements) of left atrial appendage contraction velocities measured during resumption of sinus rhythm. Increasing the duration of pacing-induced atrial fibrillation to 30–45 min resulted in a 52–62% reduction in postconversion left atrial appendage contraction velocities relative to baseline. In this study we chose to study a 60-min period of atrial fibrillation induced and maintained continuously by rapid atrial pacing. At 15-min intervals during pacing-induced atrial fibrillation, hemodynamic and pulsed Doppler measurements were obtained. At the end of the 60-min period of pacing-induced atrial fibrillation, rapid atrial pacing was abruptly terminated resulting in spontaneous resumption of sinus rhythm within 1–5 min.

As soon as sinus rhythm resumed, atrioventricular sequential pacing was begun at settings identical to those used during the baseline period. Hemodynamic and pulsed Doppler measurements during atrioventricular sequential pacing were made at the time of termination of atrial fibrillation and at 10-min intervals thereafter.

**Doppler echocardiographic measurements.** The pulsed-wave Doppler spectra were recorded on 1.27-cm VHS videotape and played back on a dedicated off-line image analysis work station (Nova Microsonics, Allendale, NJ) for quantitation. The envelope of the left atrial appendage flow velocity profile was digitized along its outer edge (representing the instantaneous time-varying maximal flow velocities). In sinus rhythm during atrioventricular sequential pacing (at baseline and after termination of atrial fibrillation) a typical quadrifasic wave form was recorded. The first and second positive waveforms represent, respectively (19,20): 1) the passive emptying of the left atrial appendage during early diastolic left ventricular filling, and 2) the active emptying of the left atrial appendage after the electrocardiographic p wave. It is the peak velocity of this later waveform that was averaged over five cycles and identified as the left atrial appendage contraction velocity. In atrial fibrillation, repetitive positive left atrial appendage velocities representing appendage emptying during atrial fibrillation were recorded. These left atrial appendage emptying velocities during atrial fibrillation are highly irregular in amplitude and frequency. To characterize their average magnitude, the peak velocities from 20 consecutive waveforms were measured and averaged to provide an index of the amplitude of these waveforms during atrial fibrillation.

The envelope of the transmital flow velocity profile was also digitized along its outer edge. The transmital flow velocity profile is comprised of an early diastolic waveform representing early filling of the left ventricle and a later diastolic waveform representing active left atrial contraction. In sinus rhythm during atrioventricular sequential pacing (at baseline and after termination of atrial fibrillation) the peak velocity of left atrial contraction was measured and averaged over five cycles.

**Data analysis.** Serial comparisons of a given variable measured at specified time intervals were analyzed with a two-way analysis of variance and the Newman-Keuls correction for multiple comparisons. A p < 0.05 was considered statistically significant. All data are presented as mean values ± 1 SD.

**Results**

**Hemodynamic conditions.** Hemodynamic parameters were stable throughout the study and did not change significantly during baseline measurements, atrial fibrillation or the postatrial fibrillation recovery period. For instance, the average ventricular response during atrial fibrillation (88 ± 52 beats/min) was similar to the ventricular rates during atrioventricular sequential pacing before and after atrial fibrillation (87 ± 21 beats/min). There were no significant differences before, during and after atrial fibrillation in mean arterial pressure (119 ± 21 vs. 114 ± 26 vs. 115 ± 33 mm Hg), cardiac output (1.8 ± 0.6 vs. 1.3 ± 0.6 vs. 1.5 ± 0.5 liters/min), mean pulmonary artery
pressure (16 ± 2 vs. 15 ± 3 vs. 14 ± 3 mm Hg), mean right atrial pressure (4 ± 2 vs. 5 ± 2 vs. 4 ± 3 mm Hg), or mean left atrial pressure (12 ± 5 vs. 12 ± 5 vs. 9 ± 6 mm Hg).

**Transmitral flow velocities.** In the baseline state during atrioventricular sequential pacing the peak velocity of left atrial contraction was 47 ± 28 cm/s. During atrial fibrillation induced by rapid atrial pacing no discernible forward transmitral flow attributable to atrial contraction could be measured. The only forward transmitral velocities recorded were the early diastolic left ventricular filling velocities. Upon conversion of atrial fibrillation to sinus rhythm, the peak velocity of atrial contraction during atrial ventricular sequential pacing was 28 ± 10 cm/s, which was significantly decreased (p < 0.02) relative to baseline measurements (Fig. 1).

**Left atrial appendage velocities.** In the baseline state during atrioventricular sequential pacing, the peak left atrial appendage contraction velocity was 58 ± 23 cm/s. During atrial fibrillation induced by rapid atrial pacing, chaotic waveforms with widely varying amplitude and cycle length were recorded from the left atrial appendage. These left atrial appendage emptying velocities exhibited an average amplitude of 22 ± 7 cm/s, which was significantly lower (p < 0.0005) than the left atrial appendage contraction velocities measured at baseline. Upon conversion of left atrial fibrillation to sinus rhythm, the peak velocity of atrial appendage contraction during atrioventricular sequential pacing was 30 ± 22 cm/s, which was significantly decreased (p < 0.001) compared with measurements at baseline (Fig. 2).

**Recovery of left atrial contraction velocities and left atrial appendage contraction velocities.** In Figure 3, left atrial contraction velocities measured from the transmitral flow velocity profile are expressed as a percent of baseline measurements for sequential 10-min intervals after the conversion from atrial fibrillation to sinus rhythm. Immediately after conversion from atrial fibrillation to sinus rhythm, the transmitral left atrial contraction velocities are reduced to 65 ± 22% of baseline values and return towards baseline values by 20 min after conversion to sinus rhythm. In Figure 4, left atrial appendage contraction velocities are expressed as percent of baseline measurements for sequential 10-min intervals after conversion from atrial fibrillation to sinus rhythm. Immediately after conversion from atrial fibrillation to sinus rhythm, the left atrial appendage contraction velocities are reduced to 49 ± 24% of baseline values. There is a progressive recovery of left atrial appendage contraction velocities to baseline levels by 40 min after conversion to sinus rhythm. An example of

**Figure 1.** Peak velocity of left atrial contraction (mitral A velocity) measured by epicardial pulsed Doppler with sample volume positioned at the mitral leaflet tips in the baseline state before atrial fibrillation (Pre AF) and immediately after reversion to sinus rhythm (Post AF) after 60 min of atrial fibrillation. Pre AF, the peak velocity of left atrial contraction was 47 ± 28 cm/s. Post AF, the peak velocity of left atrial contraction fell significantly to 28 ± 10 cm/s (p < 0.02). Individual experiments are connected by lines. Velocity calibrations are at 20-cm/s intervals.

**Figure 2.** Peak left atrial appendage contraction velocity represented by the third component of the quadriphasic waveform measured by transesophageal Doppler with sample volume positioned 5 mm proximal to the mouth of the left atrial appendage. Left atrial appendage contraction velocity in the baseline state before atrial fibrillation (Pre AF) was 58 ± 23 cm/s. After 60 min of atrial fibrillation, peak left atrial appendage contraction velocity measured upon immediate resumption of sinus rhythm (Post AF) was significantly depressed to 30 ± 22 cm/s (p < 0.001). Individual experiments are connected by lines. Velocity calibrations are at 20-cm/s intervals.

**Figure 3.** Recovery of peak left atrial contraction velocities as a function of elapsed time after spontaneous conversion to sinus rhythm (Min. After Conversion to SR) from atrial fibrillation. For each experiment the peak left atrial contraction velocity was expressed as a percentage of baseline peak left atrial contraction velocity in sinus rhythm before the induction of atrial fibrillation (% Pre AF Mitral A Velocity). Immediately after conversion to sinus rhythm peak left atrial contraction velocities were significantly reduced to 65 ± 22% (p < 0.02) of baseline values and recovered to basal values over the ensuing 20 min.
Discussion

Relationship of the canine model to prior clinical studies. Transesophageal Doppler echocardiographic observations in patients undergoing cardioversion from atrial fibrillation have demonstrated a transient but profound disorder of left atrial mechanical function despite resumption of apparently normal electrical atrial activation. The present study provides a model for studying left atrial contraction velocities and left atrial appendage contraction velocities as indices of global left atrial systolic function and left atrial appendage systolic function after conversion of atrial fibrillation to sinus rhythm. Unique advantages of the model include the ability to perform reference measurements during a baseline period before the induction of atrial fibrillation, which then serve as the basis for quantifying the magnitude of left atrial mechanical stunning in the postconversion period. Additionally, factors not generally amenable to control in prior studies of patients undergoing conversion from atrial fibrillation to sinus rhythm, such as: 1) duration of atrial fibrillation, 2) heart rate during the postconversion period and 3) cardiac loading conditions, were controlled in our model. In particular, the impact of left atrial pressure on left atrial appendage contraction velocities (23) was held constant in our model. In addition, this model obviated the extraneous influences of direct current shock and antiarrhythmic drugs by examining the effect of spontaneous reversion of atrial fibrillation to sinus rhythm.

Mechanical “stunning” of the left atrium and the left atrial appendage. The salient observations from the current study are that both global left atrial systolic function and left atrial appendage systolic function are significantly depressed after spontaneous reversion of atrial fibrillation to sinus rhythm. Of particular note, the magnitude of mechanical “stunning” appears to be selectively greater for the left atrial appendage than it is for the left atrium as a whole. Upon initial reversion from atrial fibrillation to sinus rhythm, left atrial appendage contraction velocities were $49 \pm 24\%$ of baseline values ($p < 0.001$) and recovered to basal values over the ensuing 40 min.

Sequential measurements of left atrial appendage contraction velocities after conversion from atrial fibrillation to sinus rhythm in a single experiment is illustrated in Figure 5.

Figure 4. Recovery of peak left atrial appendage contraction velocities as a function of elapsed time after spontaneous conversion to sinus rhythm (Min After Conversion to SR) from atrial fibrillation. For each experiment the peak left atrial appendage contraction velocity (third component of the quadriphasic waveform) in sinus rhythm before the induction of atrial fibrillation (% Pre AF LAAv Phase 3). Immediately after conversion to sinus rhythm peak left atrial appendage contraction velocities were significantly reduced to $49 \pm 24\%$ of baseline values ($p < 0.001$) and recovered to basal values over the ensuing 40 min.

Figure 5. Pulsed Doppler recording of left atrial appendage flow velocities obtained sequentially after spontaneous conversion to sinus rhythm from atrial fibrillation in a single experiment. After the P wave of the electrocardiogram (ECG) during atrioventricular sequential overdrive pacing of sinus rhythm, the left atrial appendage contraction velocity (third component of the quadriphasic waveform) is identified by an arrow in each panel. A, 0 min (immediately after conversion from atrial fibrillation to sinus rhythm. B, 10 min after conversion. C, 20 min after conversion. D, 40 min after conversion. Note the progressive increase in the amplitude of the left atrial appendage contraction velocity (arrows) as the left atrial appendage recovers from “mechanical stunning.” In contrast, the first component (early diastolic left atrial appendage emptying velocity) of the quadriphasic waveform remains relatively constant in amplitude throughout the 40-min recovery period. Velocity calibrations are at 20-cm/s intervals. Time calibrations are at 200-ms intervals.
(arrowheads), which occurs during successive intervals during recovery, is accompanied by no corresponding change in the first positive waveform of the quadriphasic signal. The first positive waveform reflects early passive emptying of the left atrial appendage into the left atrium and ultimately across the open mitral valve into the left ventricle. These findings suggest that whereas determinants of passive emptying of the left atrial appendage are constant during the postconversion recovery period, “stunning” of active left atrial appendage contraction progressively decreases over the same interval.

Divergence in behavior of the left atrial appendage compared with the entire left atrium may be related to intrinsic differences in left atrial appendage distensibility and shortening (23). Previous investigators have postulated that abnormal transsarcolemmal fluxes of calcium during atrial fibrillation may provide a mechanism for postfibrillation atrial systolic stunning (1,5,6). We are not aware of studies examining potential differences in calcium handling by atrial myocytes from the body of the left atrium and from the left atrial appendage during atrial fibrillation. The reduction in left atrial appendage contraction velocities has previously been identified as a risk factor for thrombus formation within the left atrial appendage. Taken collectively, these observations suggest that the more prolonged stunning of the left atrial appendage postfibrillation may render it a site of predilection for thrombus formation. Chronic models of atrial fibrillation must be studied to determine whether or not the resumption of atrial fibrillation within the left atrial appendage are constant during the postconversion recovery period. The reduction in left atrial appendage function following electrical conversion of atrial dysrhythmias may provide a mechanism for postfibrillation atrial systolic stunning (1,5,6).

References