The Effects of Atrial Fibrillation on Atrial Pressure-Volume and Flow Relationships

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SUMMARY. To study whether atrial fibrillation might produce local changes in the atrium which could facilitate the tendency of this arrhythmia to become chronic and self-perpetuating, we compared the effect of atrial fibrillation, atrial pacing, and acute volume loading on the perfusion and oxygen consumption of the atrium in anesthetized dogs. Measurement of atrial perfusion with microspheres indicates that during atrial fibrillation, atrial blood flow increases 2- to 3-fold. Right atrial pacing is a significantly less potent metabolic stimulus for atrial vasodilation. Using Doppler velocity recordings of sinus node artery blood flow velocity, a marked increase in velocity is observed within 5 seconds after the initiation of atrial fibrillation. During atrial fibrillation, the sinus node artery reactive hyperemia response is markedly attenuated. Atrial fibrillation acutely decreases atrial distensibility; atrial pressure increased 81 ± 19% with only a small increase (9.7 ± 3%) in atrial diameter measured by echocardiography. During sinus rhythm, volume expansion to equivalent levels of atrial pressure as seen during atrial fibrillation increased atrial diameter 21 ± 5% P < 0.05. Atrial oxygen consumption determined by the microspectrophotometric method markedly increases during atrial fibrillation, compared to control conditions (12.3 ± 2.8 vs. 3.9 ± 0.6 ml O2/min per 100 g, respectively) P < 0.05. Atrial O2 extraction was 5.5 ± 0.4 ml O2/ml blood in the control state, and did not change with interventions. There was a linear relationship between left atrial O2 consumption and blood flow in all experimental conditions. Atrial fibrillation therefore alters atrial hemodynamics and metabolism by increasing atrial blood flow and oxygen consumption and decreasing atrial distensibility. Since atrial perfusion during atrial fibrillation is high and atrial flow reserve is limited, it is possible that additional atrial metabolic requirements might lead to atrial ischemia, fibrosis, and, thereby, perpetuation of the arrhythmia. (Circ Res 51: 205–215, 1982)

ATRIAL fibrillation, the most common chronically sustained arrhythmia that occurs in humans, has many adverse effects upon the circulation. Atrial fibrillation decreases cardiac output (McIntosh and Morris, 1966), increases susceptibility to peripheral or pulmonary emboli (Hinton et al., 1977), predisposes to AV valvular regurgitation (Müller and Shillingford, 1954), and is usually associated with a rapid ventricular response (Witherbee et al., 1952) at rest and during mild exercise. Although many previous investigators have evaluated the consequences of this arrhythmia on the systemic circulation (Greenfield et al., 1968; Dodge et al., 1957, Gilbert et al., 1963) there are no data on the effects of atrial fibrillation upon the perfusion and oxygen consumption of the atrium itself.

Early investigators who measured myocardial blood flow in conscious and anesthetized dogs with microspheres (Maclean et al., 1961, and Domenech et al., 1969) and diffusible indicators (Love and O’Meallie, 1963) reported that flow to the atria averaged 7.1 to 16.5% of total coronary blood flow. In preliminary experiments, we confirmed these findings but noted that during atrial fibrillation atrial blood flow increased 2- to 3-fold. This study therefore was designed to investigate the hemodynamic and metabolic consequences of acute atrial fibrillation on the atrium, and in particular to determine the mechanism of the increase in atrial flow seen in this arrhythmia. We evaluated the effects of atrial fibrillation on atrial pressure, dimensions, blood flow, oxygen extraction, and oxygen consumption, and compared changes in these parameters to those seen during other conditions of increased atrial metabolism: rapid atrial pacing and atrial volume expansion.

Methods

Animal Preparation

Adult mongrel dogs of both sexes (weight = 15 to 25 kg) were anesthetized with intravenous alpha chloralose (50 mg/kg) and urethane (500 mg/kg). The dogs were ventilated via a cuffed endotracheal tube with room air and supplemental oxygen. Respiratory rate, tidal volume, and supplemental oxygen were adjusted to maintain normal arterial blood gases and pH. Periodically, the lungs were hyperinflated to prevent atelectasis. The electrocardiogram was recorded from standard leads and heart rate calculated with a tachometer. Catheters were placed in a brachial and both femoral arteries for withdrawal of reference arterial blood samples and measurement of arterial pressure. All pressures were measured with Statham P23Db strain gauges. All signals were recorded on a direct-writing recorder. Follow-
ing a thoracotomy, catheters were placed in the right and/or left atria directly via an incision in the atrial appendage.

Measurement of Blood Flow

To measure flow to the atria and ventricles, we used microspheres (7–10 μm) labeled with 40Sc, 85Sr, 89Nb, 125I, and 141Ce supplied by the 3M company. For each flow measurement between 1.3 and 2.0 × 106, tracer microspheres suspended in 0.5 ml of saline were used. Before injection, the vial containing the microspheres and one drop of polysorbate 80 (Tween 80) was vigorously agitated for 4 minutes. Microscopic examination showed that 98% of the spheres were completely dispersed. Infrequent groups of 3–5 spheres were observed. Starting 1 minute before injection and continuing until 3 minutes after injection, blood was withdrawn simultaneously from a brachial and femoral artery into glass syringes with a Harvard pump at 2.06 ml/min. The microspheres were injected into the left atrial cannula over 15 seconds, and the cannula was flushed with 5 ml of saline at 37° during the subsequent 20 seconds. Following the study, the animals were killed with an injection of potassium chloride. Atrial and ventricular myocardial samples (average weight 0.74 ± 0.3 g) were taken. A large segment of the body of the atrium adjacent to but not including the atrial septum was used for the atrial samples. Single tissue specimens from the right and left ventricular free walls were used for the ventricular samples. The segments were weighed to the nearest milligram, placed in glass tubes containing 10% formalin, and counted for 5 minutes in the gamma counter. Reference blood samples were emptied into several counting tubes and the aspirating glass tubes containing 10% formalin, and counted for 5 minutes in the gamma counter. Reference blood samples were averaged. We eliminated those experiments (n = 3) where differences in the femoral and brachial reference counts were greater than 25%.

Isotope separation was accomplished by differential spectroscopy according to the method of Rudolph and Heyman (1967). The energy windows utilized were: 40Sc, 400–750 keV; 85Sr, 325–400 keV; 89Nb, 200–275 keV; 125I, 65–80 keV; 141Ce, 10–18 keV. Blood flow was calculated by using the formula MBF = CM × 100 × RBF + CR where MBF = myocardial blood flow in ml/min × 100 g, CM = counts/1 g of myocardium, RBF = reference blood flow, and CR = total counts in the reference blood.

Electrical Stimulation of the Atrium

Atrial fibrillation was induced by bipolar electrical stimulation (1 msec duration, 18–20 Hz, at voltages only slightly above capture threshold) of the right atrium via electrodes clipped to the right atrial appendage. Electrical stimulation was maintained constantly for 15 minutes prior to any intervention. Preliminary experiments showed that constant electrical stimulation was necessary to produce stable atrial fibrillation in most dogs. In a few dogs, however, stable atrial fibrillation persisted after cessation of electrical stimulating activity. In these dogs, the blood flow during spontaneous atrial fibrillation was compared to that seen during electrically maintained atrial fibrillation. Atrial blood flow in atrial fibrillation was also compared to that seen during 15 minutes of right atrial pacing (1 msec, voltage slightly above threshold) at 218 beats/min.

Alterations in Atrial Pressure and Volume

Alterations in atrial pressure and volume were achieved by inducing atrial fibrillation or by acute volume loading with autologous blood and/or saline. In each dog we matched the atrial pressure which occurred during atrial fibrillation with volume expansion (high level) during sinus rhythm. In addition, in some animals, an intermediate level of volume expansion also was produced. In the first series of nine dogs, both right and left atrial pressures were recorded. For all subsequent experiments, only the left atrial pressure was measured.

To compare the relative magnitude of the major determinants for atrial oxygen consumption during atrial fibrillation and volume expansion, we calculated an index of passive atrial wall stress by multiplying the maximum left atrial diameter by the mean left atrial pressure. Atrial pressure-volume relationships were compared by two methods. First, using each dog as its own control, percent change in left atrial pressure and diameter for each intervention was calculated and then averaged for the three groups.

Second, to calculate differences in atrial stiffness in the fibrillating and the expanded atrium, atrial distensibility in each condition was calculated according to the formula, D = Δd/ΔP - Δd, where D is the atrial distensibility, Δd is the echocardiographically determined change in atrial diameter, di is the initial atrial diameter, and ΔP is the change in atrial pressure.

Measurement of Left Atrial Diameter and Cross-Sectional Area

The anteroposterior diameter of the left atrium was visualized by means of an M-mode ultrasound transducer affixed lightly to the anterior surface of the heart by a mechanical arm, which eliminated transducer motion. The ultrasonic beam was directed toward the base of the heart to traverse the aortic root. During volume expansion, the transducer was raised, if necessary, to avoid compressing the heart and artificially reducing atrial diameter. The aortic valve was used as an internal landmark to maintain a constant beam orientation throughout the study. Confirmation of left atrial chamber identification on the echocardiograms was achieved by observing ultrasonic contrast echos in the left atrium when cardiogreen dye was injected directly into the left atrium through the left atrial catheter (Kerber et al., 1974). Changes in atrial diameter to the nearest millimeter were measured during control conditions, during atrial fibrillation, and volume loading.

To ascertain the relationship between changes in atrial diameter seen with M-mode echocardiography and changes in atrial cross-sectional area produced by the interventions, two-dimensional ultrasonic tomographic cross-sections were recorded in three animals. Sections of the left atrium oriented 90° to each other in long and short cardiac axis views were obtained using a Toshiba SSH-10 array two-dimensional ultrasonicoscope, and recorded on a video tape recorder. The images were analyzed by tracing the atrial circumference from the frozen-frame videotape images. End-systolic (peak of EKG T-wave) images were analyzed in each axis. The resulting tracing was planimetered and corrected for magnification so that maximal atrial areas in both long and short axis planes were obtained (see Fig. 6).

Doppler Measurements of Atrial Blood Flow Velocity

A modified Doppler velocity probe recently developed and validated in our laboratory (Marcus et al., 1981) was used to measure blood flow velocity in the sinus node artery. The ultrasonic probe consists of a 1 mm in diameter piezoelectric crystal attached at a 45° angle to a 4-mm silicone cup. The wires from the crystal and a small tube for applying suction exit from the top of the probe. When
this probe is placed on a coronary vessel, the angle between the crystal and the coronary vessel is about 45°, which is optimal for detecting a Doppler shift.

Phasic and mean blood flow velocity in the sinus node artery were recorded under control conditions and during atrial fibrillation. Continuous measurements of coronary flow velocity in the atrium therefore could be made. Changes in blood flow velocity in the sinus node artery were measured following transient 10-, 15-, and 20-second occlusions of the sinus node artery during sinus rhythm and during atrial fibrillation. Since no significant differences were noted between occlusions of 10- to 20-second duration, only responses to 15-second occlusions are included.

Atrial Oxygen Extraction and Consumption

To measure oxygen consumption of the atrium, a recently developed microspectrophotometric method for determining O2 saturation in frozen atrial arterial and venous blood vessels was coupled with measurements of atrial perfusion obtained using microsphere injections (Sinha et al., 1975, 1977).

Following the blood flow measurements, the left atrium was quickly excised with a large pair of shears and divided in half. Within 5 seconds, the atrial appendage and half of the adjacent atrial body were placed in liquid nitrogen. The remaining half of the left atrium was used for microsphere determinations. All tissue was kept frozen in liquid nitrogen until the time of the analysis.

Two portions of the frozen tissue were analyzed: the atrial appendage and the adjacent half of the body of the left atrium. The tissue was cut on a band saw at —20°C, and mounted with an embedding medium. Thirty-micrometer sections were cut on a rotary microtome at —20°C and mounted with an embedding medium. Thirty-micrometer sections were cut on a rotary microtome at —20°C and mounted with an embedding medium. Thirty-micrometer sections were cut on a rotary microtome at —20°C and mounted with an embedding medium. Thirty-micrometer sections were cut on a rotary microtome at —20°C and mounted with an embedding medium.

Measurements of O2 saturation and diameter were made for each vessel examined. An average of three arteries and eight veins per sample were analyzed. The O2 content of the blood was obtained by multiplying the percent O2 saturation by the hemoglobin concentration times 1.36. Oxygen extraction was calculated as the difference between the average arterial and venous O2 content. The product of O2 extraction and blood flow was used to determine atrial oxygen consumption according to the Fick principle.

Protocols

We performed four groups of experiments (the first and third groups consisted of two parts).

Group 1:

Atrial Pacing vs. Atrial Fibrillation—Effects on right and left atrial pressure and flow. In nine dogs, the effects of atrial fibrillation and rapid atrial pacing on atrial perfusion were studied. Measurements of right and left atrial pressure and perfusion, and right and left ventricular perfusion, were made during the following conditions: (a) control, (b) atrial pacing (atrial rate 218 beats/min), (c) a second control period, and (d) atrial fibrillation.

Electrically Sustained vs. Spontaneous Atrial Fibrillation—Effects on right and left atrial pressure and flow. In four dogs, stable atrial fibrillation persisted after cessation of the electrical fibrillatory stimulus. Additional pressure and flow measurements were made following 15 minutes of this spontaneous fibrillation. In this protocol and those that follow, conditions during each intervention were stable for 15 minutes before measurements were obtained.

Group 2:

Effects of Atrial Fibrillation on Doppler Measurements of Sinus Node Artery Flow Velocity. To determine the time course of changes in atrial flow after the onset of atrial fibrillation, we measured sinus node artery blood flow velocity continuously during control conditions and after atrial fibrillation in four dogs. Reactive hyperemia responses in the sinus node artery were obtained during both conditions to assess coronary dilator reserve.

Group 3:

Atrial Fibrillation vs. Atrial Volume Expansion—Effects on left atrial pressure, flow, diameter, wall stress, and distensibility. To determine the mechanism responsible for changes in atrial flow seen during atrial fibrillation, we obtained measurements of left atrial pressure, diameter and perfusion in 21 dogs both during control conditions and after 15 minutes of atrial fibrillation. In 15 of these animals, atrial volume expansion was performed to levels of atrial pressure equivalent to that seen during atrial fibrillation. In a small subgroup (o) of the volume-expanded animals, atrial diameter and pressure were recorded at an intermediate (lower) level of volume expansion. All of the animals in the two volume-expanded subgroups were used in the calculations of atrial distensibility.

Atrial Fibrillation vs. Atrial Volume Expansion—Effects on left atrial pressure and cross-sectional area. To be certain that changes in atrial diameter measured with M-mode echo reflect changes in atrial volume, atrial cross-sectional area was determined in two perpendicular tomographic cross-sections during control conditions, atrial fibrillation, volume expansion to equivalent atrial pressures (average transfusion volume 350 ml) and a second higher level of volume expansion (average transfusion volume 700 ml) in three dogs.

Group 4:

Sinus Rhythm, Atrial Fibrillation, and Atrial Volume Expansion—Effects on atrial O2 extraction and consumption. To determine whether changes in atrial perfusion during atrial fibrillation and volume expansion reflect changes in atrial oxygen consumption, left atrial oxygen extraction, perfusion, pressure, and diameter were measured in the following experiments: control (n = 5); atrial fibrillation (n = 7); and atrial volume expansion (high level) (n = 6). A 15-minute period of atrial fibrillation preceded the volume expansion experiments in these six dogs.

Statistical Analysis

Statistical analysis of the data was obtained using an analysis of variance with Tukey’s multiple comparison, or when appropriate, a paired t-test. Values are expressed as the mean ± 1 SEM. A P value of <0.05 was accepted as significant.

Results

Effects of Atrial Fibrillation on Atrial Blood Flow

Atrial flow and pressure markedly increased during atrial fibrillation (Fig. 1). During control conditions, left atrial flow averaged 57 ± 6 ml/min per 100 g, and
Mean Atrial Flow ml/min/100gm

Mean Atrial Pressure mmHg

FIGURE 1. Effects of atrial pacing and atrial fibrillation on mean atrial pressure and atrial blood flow. Values are ± 1 SEM. Integers under the bars indicate number of experiments in each group. Atrial pacing increased the heart rate from 169 ± 9 to 218 beats/min. The ventricular rate during atrial fibrillation averaged 273 ± 11 beats/min. Significant increases (P < 0.05) in atrial pressure and flow in both atria were seen during atrial fibrillation.

flow to the right and left ventricles averaged 107 ± 15 and 139 ± 22 ml/min per 100 g, respectively. Total flow to both atria increased from 6% of total coronary blood flow during sinus rhythm to 13% during atrial fibrillation. Mean aortic pressure decreased from 108 ± 8 (control) to 93 ± 6 mm Hg during atrial fibrillation. Right and left ventricular blood flow during atrial fibrillation increased only modestly despite an increased ventricular rate. Flow per gram to the atrial myocardium during atrial fibrillation exceeded left ventricular flow per gram. Increasing atrial rate with pacing from 169 ± 9 to 218 beats/min was associated with only modest increases in atrial blood flow (Fig. 1). The effects of electrically maintained and spontaneous atrial fibrillation on atrial flow and pressure were similar (Fig. 2).

Effects of Atrial Fibrillation on the Reactive Hyperemia Response after Transient Occlusion of the Sinus Node Artery

Phasic blood flow velocity in the sinus node artery was primarily systolic (Fig. 3). During sinus rhythm, release of a 15-second arterial occlusion of the sinus node artery produced a moderate increase in the sinus node artery blood flow velocity with a peak-to-resting velocity ratio of 3.4 ± 0.3/1. Within 5 seconds after electrical induction of atrial fibrillation, mean blood flow velocity in the sinus node artery increased (Fig. 3). The peak blood flow velocity response occurred in less than 1 minute. During atrial fibrillation, the reactive hyperemia response was markedly attenuated. Release of a 15-second occlusion of the sinus node artery during atrial fibrillation resulted in a peak-to-resting velocity ratio of 1.9 ± 0.3/1 (P < 0.05). In two of four dogs studied during atrial fibrillation, the peak-to-resting velocity ratio was nearly abolished (<1.2/1).

Changes in Left Atrial Pressure-Volume Relationships during Atrial Fibrillation and Volume Expansion

During atrial fibrillation, left atrial blood flow increased from 2- to 3-fold (protocol 3A). Atrial fibrillation resulted in a small and insignificant increase (1.4 ± 1.5 mm) in left atrial diameter. However, left atrial pressure rose to almost twice its control value (Figs. 4 and 5). The calculated passive atrial wall stress index was increased significantly during both atrial fibrillation and high level volume expansion. Despite increasing left atrial pressure to levels similar to those observed during atrial fibrillation and a greater increase in left atrial diameter, the increase in left atrial blood flow during volume expansion was significantly less than that which occurred during atrial fibrillation (Fig. 4).

In that subgroup of animals in which the effects of atrial fibrillation on atrial pressure and diameter were compared, left atrial pressure averaged 4.6 ± 0.9 mm Hg and left atrial diameter was 25 ± 0.4 mm prior to atrial fibrillation. During atrial fibrillation, a small increase in diameter (9.7 ± 3%) was associated with a marked increase in pressure (81 ± 19%). Before volume expansion, the left atrial pressure and diameter were similar to the initial control state (4.9 ± 0.7 mm Hg and 22 ± 0.2 mm, respectively). With modest volume expansion (n = 6), left atrial pressure rose to a level similar to that seen during atrial fibrillation (78 ± 23%), but the change in left atrial diameter was significantly greater (21 ± 5%) (P < 0.05). With additional volume expansion, left atrial pressure increased by 125 ± 20% and left atrial diameter by 27 ± 8%. Calculated atrial distensibility averaged 0.047 ± 0.02 mm Hg⁻¹ during atrial fibrillation, 0.11 ± 0.04 mm Hg⁻¹ during the intermediate level of volume loading, and 0.078 ± 0.03 mm Hg⁻¹ during volume loading to equivalent atrial pressures as seen during
atrial fibrillation (P < 0.05 atrial fibrillation vs. volume loading, both levels). Thus, in atrial fibrillation, the distensibility of the atrium is decreased.

To be certain that changes in atrial diameter during volume expansion and atrial fibrillation as measured with single plane M-mode echocardiograms were an adequate reflection of changes occurring in the volume of left atrium during these interventions, we recorded left atrial tomographic cross-sections in both long and short axis views, using two-dimensional echocardiography in three additional animals (protocol 3B). Atrial pressure in these three dogs averaged 7.7 ± 1.2 mm Hg control and 9.3 ± 1.2 during atrial fibrillation. With the animals in sinus rhythm, the first level of volume expansion produced an equivalent atrial pressure (9.2 ± 1.1 mm Hg) to that seen during atrial fibrillation. During the second higher level of volume expansion (also performed during sinus rhythm), atrial pressure increased to 11.7 ± 0.7 mm Hg. Maximum atrial cross-sectional area in the control state was 3.2 ± 0.1 cm² long axis, 4.3 ± 0.4 cm² short axis. During atrial fibrillation, the long axis area decreased 9% to 2.9 ± 0.4 cm², whereas the short axis area increased 10% to 4.7 ± 0.4 cm². Thus it is reasonable to predict that during atrial fibrillation, changes in left atrial volume were minimal. Volume expansion to equivalent pressures, however, resulted in ≥10% increase in atrial areas in both planes. Low

![Diagram](image-url)

**Figure 3.** Phasic and mean Doppler blood flow velocity measurements during sinus rhythm and following the onset of atrial fibrillation. Release of a transient occlusion of the sinus node artery during control conditions resulted in a peak-to-resting blood flow velocity ratio of 3.4/1. The increase in atrial blood flow velocity during atrial fibrillation was gradual, having an onset within 5 seconds. After 15 minutes of atrial fibrillation, the reactive hyperemia response of this atrial artery was severely attenuated.
FIGURE 4. Left atrial pressure, volume, flow, and wall stress relationships during control conditions, atrial fibrillation, and with volume expansion. The average heart rates were 149 ± 15, 204 ± 15, and 129 ± 6 beats/min, respectively, in the three conditions. Mean arterial pressure was 84 ± 5, 81 ± 4, and 117 ± 5 mm Hg. Atrial fibrillation resulted in significant increases in atrial pressure, flow and wall stress index. Despite a greater wall stress index during volume expansion than in atrial fibrillation, atrial blood flow was significantly less.

level volume expansion increased the atrial area from 3.1 ± 0.1 to 3.5 ± 0.3 cm² long axis; 4.9 ± 0.3 to 5.4 ± 0.5 cm² short axis (Fig. 6). The higher level of volume expansion increased the atrial area an additional 42% in the long axis and 28% in the short axis views.

Thus, whereas atrial fibrillation resulted in no significant change in atrial area, volume expansion to equal atrial pressures caused increases in atrial area in both long and short axes.

**Effect of Atrial Fibrillation and Volume Expansion on Atrial Oxygen Extraction and Consumption**

Left atrial oxygen extraction (C\(_{aO_2}\) - C\(_{vO_2}\)) measurements during control conditions, atrial fibrillation, and high levels of volume expansion were similar (Fig. 7). The atrial arterial oxygen saturation averaged 87 ± 1.5% under control conditions and was not significantly changed during atrial fibrillation or volume expansion. Atrial venous oxygen saturation was 61 ± 1% in the control condition, 56 ± 1% with atrial fibrillation, and 59 ± 1% during volume expansion.

The diameter of the arteries and veins examined were: 86 ± 17 and 40 ± 4 μm, respectively, during control conditions; 56 ± 4 and 57 ± 7 μm, respectively, during atrial fibrillations; and 71 ± 9 and 49 ± 4 μm, respectively, during volume expansion. There were no significant differences between the results obtained in samples from the left atrial body or atrial appendage. Hemoglobin determinations averaged 13.5 ± 0.3, 12.9 ± 0.3, and 13.7 ± 0.4 g% during control conditions, atrial fibrillation and volume expansion, respectively.

In these experiments, left atrial blood flow (Q) increased 3-fold during atrial fibrillation but did not significantly change during volume expansion. Left atrial oxygen consumption increased 3-fold during atrial fibrillation but did not change during volume expansion (Fig. 7). There was a linear relationship between left atrial flow and oxygen consumption (r = 0.95) during the three different experimental conditions (Fig. 8).

**Discussion**

This investigation provides the first systematic study of the effects of atrial fibrillation on the perfusion and oxygen consumption of the atrium. In addition to attaining new information regarding this specific arrhythmia, atrial fibrillation was used as a tool to investigate atrial physiology and metabolism. There are several new observations: (1) During the fibrillatory state, there is a 2- to 3-fold increase in
blood flow to both atria. During atrial fibrillation, flow per gram to the atrial myocardium exceeds left ventricular flow per gram. (2) With the onset of atrial fibrillation, atrial blood flow velocity rises promptly and there is marked attenuation in the reactive hyperemia response of sinus node artery. (3) Atrial fibrillation acutely decreases left atrial distensibility. (4) Oxygen consumption during atrial fibrillation is markedly increased. This increase is disproportionately greater than the increase in passive wall stress resulting from increased atrial pressure and volume, and implies that during atrial fibrillation the active tension generated by the fibrillating muscle is a major determinant of atrial oxygen consumption.

In these studies we employed three new methods to assess atrial hemodynamics and metabolism: measurement of atrial tissue oxygen consumption using a "micro-Fick" technique, Doppler measurement of sinus node artery velocity, and a wall stress index designed to estimate passive atrial wall stress under varying conditions.

The recently developed microspectrophotometric method for determining \(O_2\) saturation in frozen arteries and veins was used for calculations of atrial oxygen extraction (Sinha et al., 1975; Sinha et al., 1977). The accuracy of \(O_2\) saturation determinations by this method has been shown to be about 4% when compared to the Van Slyke method (Weiss et al., 1978). Accurate determinations of \(O_2\) saturation in small vessels are dependent upon (1) a very rapid freeze time, (2) correct identification of arteries and veins, and (3) the assumption that only oxy- and deoxygenated hemoglobin are present. The short time from tissue excision until freezing (5 seconds), coupled with the thinness of the tissue samples, make this method ideal for the study of the oxygen consumption of the atrium. Another potential methodological problem, the decreasing venous oxygen saturation with increasing tissue depth (Weiss and Sinha, 1978), is also minimized due to the thin atrial samples. Although arterial oxygen saturation within each animal was relatively uniform, (so 5%) venous saturation exhibited considerable variability (so 20%). This variability in venous oxygen saturation reflects heterogeneous tissue flow (Falsetti et al., 1975) and oxygen consumption rather than experimental error.

To study changes in \(O_2\) extraction in the presence of this heterogeneity in venous \(O_2\) saturations, we averaged the first 8 veins in the 20–200 \(\mu m\) range per sample for analysis. Care was taken to ensure that the
arterial $P_{O_2}$ was not greater than 100 mm Hg. Under the experimental conditions in this study, abnormal hemoglobin molecules were unlikely to be present. Thus the criteria for accurate $O_2$ saturation determinations by this method are fulfilled in this study.

The Doppler velocity probe we employed has recently been developed and validated in our laboratory. In previous studies using a wide variety of hemodynamic perturbations, we have shown that mean coronary flow is highly correlated with mean coronary velocity ($r = 0.97$) (Marcus et al., 1981). Recordings of phasic coronary velocity and flow and the reactive hyperemia response obtained with the Doppler and electromagnetic flow meters are nearly indistinguishable. In this study, the Doppler probe was applied to the sinus node artery. Previous investigations in our laboratory have shown that this artery supplies about 65% of flow to the anterior right atrial wall (White et al., 1977). The 15-second occlusion of this vessel needed to obtain the reactive hyperemia response did not alter atrial or arterial pressure.

In an attempt to compare wall stress in the atrium under each experimental condition, we calculated an index of atrial wall stress by multiplying atrial pressure by atrial diameter. This calculation assumes that changes in atrial wall thickness among the experimental groups are not significant, and that the volume of the atrium can be determined from a single atrial diameter. Previous studies have shown that left atrial size calculated from a single anteroposterior echocardiographic dimension correlates highly with left atrial surface area and volume as measured from selective cine angiograms (tenCate et al., 1974; Yabek et al., 1976). Since the left atrium is a relatively spherical structure, enlargement was thought to occur symmetrically (Schabelman et al., 1978). However, recent studies have challenged this and have suggested a more complex relationship between atrial diameter and volume (Schabelman et al., 1981). Therefore, we performed additional two-dimensional echocardiographic measurements of atrial area in both long and short axes to validate the use of the M-mode echo as an index of changes in atrial volume. These studies indicate that changes in atrial diameter correlate well with changes in atrial cross-sectional area. Our atrial wall stress index, however, reflects primarily differences in passive stress on the atrial wall. Any changes in active tension generated by the rapid asynchronous contractions of the fibrillating myocardium would not be included.

Thus the basic assumptions underlying the proper usage of these three new experimental methods—the
White et al./Atrial Fibrillation and Atrial Blood Flow

Why is atrial oxygen extraction less than ventricular oxygen extraction? Although oxygen consumption of the left and right ventricles differ (11 and 7.1 ml O₂/min per 100 g, respectively [Weiss et al., 1981]), oxygen extraction is similar (12.6 ml O₂/100 ml blood). In this study, left atrial oxygen consumption during sinus rhythm was 3.9 ± 0.6 ml O₂/mm per 100 g and oxygen extraction was 5.5 ± 0.4 ml O₂/100 ml blood. Thus, oxygen extraction is much less in the atrium than in the ventricles. The oxygen extraction and oxygen consumption of atrial muscle therefore appear more like that of skeletal muscle (Marcus et al., 1981) than ventricular muscle. This would appear more appropriate for the lower range of atrial metabolic demands during sinus rhythm than for the very high metabolic demands of atrial fibrillation. Even when atrial oxygen consumption was markedly augmented, oxygen extraction of the atrium did not increase. This implies that atrial muscle reacts like ventricular muscle (though at a different extraction level setpoint), meeting most increases in metabolic demand by increases in oxygen delivery rather than increasing oxygen extraction. Whether conditions of even greater atrial metabolic demand might generate increases in oxygen extraction is unknown.

Why is atrial oxygen extraction much less than ventricular oxygen extraction? Why is atrial metabolism high during atrial fibrillation? Why is atrial reactive hyperemia response decreased during atrial fibrillation? Why does atrial pressure rise during atrial fibrillation? Why is atrial oxygen extraction less than ventricular oxygen extraction? Although oxygen consumption of the left and right ventricles differ (11 and 7.1 ml O₂/min per 100 g, respectively [Weiss et al., 1981]), oxygen extraction is similar (12.6 ml O₂/100 ml blood). In this study, left atrial oxygen consumption during sinus rhythm was 3.9 ± 0.6 ml O₂/mm per 100 g and oxygen extraction was 5.5 ± 0.4 ml O₂/100 ml blood. Thus, oxygen extraction is much less in the atrium than in the ventricles. The oxygen extraction and oxygen consumption of atrial muscle therefore appear more like that of skeletal muscle (Marcus et al., 1981) than ventricular muscle. This would appear more appropriate for the lower range of atrial metabolic demands during sinus rhythm than for the very high metabolic demands of atrial fibrillation. Even when atrial oxygen consumption was markedly augmented, oxygen extraction of the atrium did not increase. This implies that atrial muscle reacts like ventricular muscle (though at a different extraction level setpoint), meeting most increases in metabolic demand by increases in oxygen delivery rather than increasing oxygen extraction. Whether conditions of even greater atrial metabolic demand might generate increases in oxygen extraction is unknown.

Why is atrial metabolism high during atrial fibrillation? During acute volume expansion, left atrial oxygen consumption was slightly but not significantly increased from control values. However, during atrial fibrillation, atrial oxygen consumption greatly increased. These findings suggest that the changes in atrial pressure and dimensions that accompany atrial fibrillation are not an adequate reflection of the true metabolic demands of the atrium during this condition. During atrial fibrillation, the frequency of atrial contraction is high, even though little external work is generated because of the asynchronous contractions.

The relationship between left atrial oxygen consumption and blood flow, whether determined during control conditions, atrial fibrillation, or volume expansion, is linear (Fig. 8). Thus the marked increases in flow during atrial fibrillation are proportionate to an increased oxygen demand and are not the result of opening of precapillary shunts representing “luxury perfusion” (Lassen, 1966). It is of interest that ventricular fibrillation is also associated with a significant increase in myocardial oxygen consumption (Hottenrott et al., 1974).

Why is the reactive hyperemia response of the atrium decreased during atrial fibrillation? Transient occlusion of the sinus artery during sinus rhythm in these studies resulted in a reactive hyperemia response increasing atrial flow approximately three times the control velocity. During atrial fibrillation, the reactive hyperemia response was significantly attenuated and in some animals nearly abolished. These findings demonstrate that flow reserve is decreased during atrial fibrillation. Our studies do not permit us to determine whether the decrease in reserve results simply from the increase in resting flow, or whether, in addition, minimal vascular resistance is decreased during atrial fibrillation.

Additional studies comparing atrial velocity and flow during atrial fibrillation to those obtained during...
infusions of dipyridamole or adenosine will be needed to answer this question.

Why does atrial pressure rise during atrial fibrillation? Although Little (1960), examining the isolated pulmonary-left heart vascular segment, described a slight (1 mm Hg) fall in atrial pressure when transient atrial fibrillation was compared to vagally induced atrial and ventricular asystole, other workers have described increases in atrial pressure during atrial fibrillation in the intact animal.

Skinner et al. (1964) noted, in dogs with surgically induced heart block and constant ventricular pacing, that atrial fibrillation resulted in an increase in atrial pressure. These investigators noted hemodynamic evidence for mild early mitral regurgitation which they felt was a contributing factor. Our data suggest that the rapid asynchronous atrial contractions, although ineffectual in generating a propagated atrial a-wave, markedly decrease the distensibility of the atrium and may contribute to an increased mean atrial pressure. The magnitude of the contribution of decreased left atrial distensibility toward increasing left ventricular filling pressure is apparent if one considers that an average transfusion volume of 675 ± 131 ml (23 ml/kg body weight) was necessary to increase atrial pressure to the same level which occurred during atrial fibrillation.

Clinical Implications

Although there are undoubtedly major differences between these acute studies in the animal model and the chronic arrhythmia as it occurs in humans, the results of these investigations could have clinical implications. In the absence of heart failure, a reduction in atrial distensibility during atrial fibrillation would seem beneficial, favoring homeostasis by tending to increase ventricular sarcomere length and thus partially compensating for the loss of atrial systole. During conditions of heart failure with maximum sarcomere length, decreased atrial distensibility during atrial fibrillation could aggravate pulmonary congestion and dyspnea by increasing pulmonary artery wedge pressure.

Persistent atrial fibrillation and the inability to maintain sinus rhythm after electrical cardioversion have been correlated with increased atrial size and prolonged duration of atrial fibrillation (Henry et al., 1976). These factors would tend to further increase the already high metabolic demands resulting from the fibrillatory state itself. If atrial fibrillation results in maximal atrial vasodilation, and if atrial \( O_2 \) extraction cannot be increased, further increases in metabolic demands might jeopardize the atrial \( O_2 \) supply/demand ratio. Ischemia, and the later development of fibrosis under conditions of chronicity, might lead to persistence of atrial fibrillation. Pathological studies have suggested that atrial fibrosis and the loss of atrial musculature are common in atrial fibrillation of long duration (Davies and Pomerance, 1972). Although demonstrated most clearly in atrial fibrillation of rheumatic etiology (Bailey et al., 1968), loss of atrial muscle, and atrial fibrosis and scarring have been demonstrated in idiopathic atrial fibrillation and in patients with hypertensive or ischemic etiologies (Davies and Pomerance, 1972).

These studies thus demonstrate that acute atrial fibrillation is associated with a decreased atrial distensibility and a marked increase in atrial perfusion and oxygen consumption resulting from increased atrial metabolic demands. Whether additional metabolic demands might eventuate in ischemia and fibrosis is at present unknown.

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White et al. / Atrial Fibrillation and Atrial Blood Flow

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