Wave intensity analysis of left atrial mechanics and energetics in anesthetized dogs

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Hobson TN, Flewitt JA, Belenkie I, Tyberg JV. Wave intensity analysis of left atrial mechanics and energetics in anesthetized dogs. Am J Physiol Heart Circ Physiol 292:H1533–H1540, 2007. First published November 17, 2006; doi:10.1152/ajpheart.00837.2006.—The left atrium (LA) functions as a booster pump during late diastole, generating the Doppler transmitral A wave and contributing incrementally to left ventricular (LV) filling. However, after volume loading and in certain disease states, LA contraction fills the LV less effectively, and retrograde flow (i.e., the Doppler Ar wave) into the pulmonary veins increases. The purpose of this study was to provide an energetic analysis of LA contraction to clarify the mechanisms responsible for changes in forward and backward flow. Wave intensity analysis was performed at the mitral valve and a pulmonary vein orifice. As operative LV stiffness increased with progressive volume loading, the reflection coefficient (i.e., energy of reflected wave/energy of incident wave) also increased. This reflected wave decelerated the forward movement of blood through the mitral valve and was transmitted through the LA, accelerating retrograde blood flow in the pulmonary veins. Although total LA work increased with volume loading, the forward hydraulic work decreased and backward hydraulic work increased. Thus wave reflection due to increased LV stiffness accounts for the decrease in the A wave and the increase in the Ar wave measured by Doppler.

hemiaodynamics; left atrium; A wave; Ar wave; Doppler echocardiography

THE LEFT ATRIUM (LA) functions as a booster pump during late diastole, contributing ~20% to left ventricular (LV) filling (32). Doppler echocardiography has shown that there can be retrograde flow (i.e., the atrial reversal or Ar wave) into the pulmonary veins (PV) as blood is propelled forward into the LV during atrial systole (i.e., the transmitral A wave) (30). Analysis of the A and Ar waves may be useful in the assessment of various cardiac conditions (11, 12, 30, 33).

Previous studies have demonstrated an inverse relationship between LV end-diastolic pressure (PVED) and forward flow during atrial systole (16, 25, 31). Increased LV operative stiffness, which is related to the increase in PVED, is recognized as one mechanism responsible for diminished atrial contribution to LV filling (32, 45) and augmented reversed flow into the PV (2, 22, 24, 32, 41). Although it is intuitive that such a relationship would exist, the fundamental mechanisms have not been studied.

Wave intensity analysis (WIA) (34, 35, 43) can be used to discriminate between the effects of upstream and downstream events at a specific location and provides a means of quantifying the energy carried by waves traveling through the heart and vasculature. A wave [i.e., a “propagated disturbance” (26)] changes both pressure (P) and blood velocity (U); wave “intensity” is an instantaneous function of the incremental changes in P and U and is expressed as power normalized by cross-sectional area (W/m²). Waves are considered to be forward-going when they travel in the direction of the net blood flow. “Compression” waves always increase P and “expansion” waves always decrease P. In the forward direction, compression waves increase U and expansion waves decrease U; in the backward direction, compression waves decrease U and expansion waves increase U.

Therefore, to assess the mechanisms responsible for diminished forward and increased backward flow with increased LV stiffness, we performed an energetic analysis of LA systole: we measured LA pressure-volume work, directional hydraulic work, and wave energy. Our results show that the increased wave reflection associated with increased LV operative stiffness is responsible for the decreased forward flow into the LV and the increased retrograde flow into the pulmonary veins.

MATERIALS AND METHODS

Animal preparation. Following a protocol approved by the Institutional Animal Care Committee, six healthy mongrel dogs (20–26 kg) were anesthetized initially with thiopental sodium (20 mg/kg) and subsequently with fentanyl citrate (30 μg·kg⁻¹·h⁻¹) and were ventilated with a 1:1 nitrous oxide-oxygen mixture. The rate of a constant-volume respirator (tidal volume, 15 ml/kg; model 607, Harvard Apparatus, Natick, MA) was adjusted to maintain normal blood gas tensions and pH. Body temperature was maintained at 37°C with a circulating water warming blanket and a heat lamp. A large-bore catheter was inserted into a jugular vein for infusion of volume (saline-Pentastarch mixture).

Pressures were measured in the LV (P_LV), aorta (P_AO), LA (P_LA), and a PV (P_PV) with the use of high-fidelity catheter-tip manometers and a 2-F micromanometer (Millar Instruments; Houston, TX), all referenced to the mid-LV plane via fluid-filled lumens and external transducers. The LV catheter was introduced through a carotid artery, the LA catheter through the appendage, and the PV catheter through a small right PV branch (the PV catheter was then threaded across the LA into an opposite PV with the aid of a stiff introducer). Ultrasonic flow probes were positioned on the proximal ascending aorta and on the downstream end of a PV (beside the one that contained the pressure transducer) and were connected to a flowmeter (Transonic Systems, Ithaca, NY). Percardial pressure (P_peric) was measured over the LA with a 2.5 × 2.5-cm flat, liquid-container balloon transducer (17). The pericardium was reapproximated and sutured following instrumentation (40). Before data collection, all pressures were matched to a reference pressure to correct for any baseline drift. A

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5-MHz transesophageal echocardiographic probe (model 77020AC; Hewlett-Packard, Palo Alto, CA) was used to obtain apical two- or four-chamber views of the heart. Mitral inflow velocity (Doppler) was measured at the tips of the mitral leaflets. Echocardiographic and hemodynamic data were synchronized using a video frame counter (MicroEmbedded Consulting, Calgary, Alberta, Canada). Data analysis was performed using specially designed software (CV Works; Advanced Measurements, Calgary, Alberta, Canada).

Two quasi-diametric LA dimensions, \(D_L\) (length) and \(D_T\) (thickness), were measured by sonomicrometry (Sonometrics, London, Ontario, Canada). \(D_L\) was defined by a pair of crystals placed across the length of the LA, one deep to the appendage at the base of the aorta and the other on the posterior (dorsal) surface of the LA, superior (cephalad) to the coronary sinus; \(D_T\) was defined by a pair of crystals placed across the thickness of the LA, one on the anterior (ventral) surface of the LA at the LA-LV border and the other on the most superior (cephalad) aspect of the LA, lateral to the aorta. Three orthogonal LV dimensions also were measured: anteroposterior (\(D_{AP}\)), base to apex (\(D_{B-A}\)), and septum to free wall (\(D_{S-F}\)). The ultrasonic signals were filtered (low pass; 20–30 Hz) and edited to eliminate artifacts due to imperfect signal reception (Cardiosoft; Sonometrics).

**Experimental protocol.** The animals were volume-loaded to relate LA pressure-volume work, forward and backward hydraulic work, and wave energy to LV operative stiffness throughout a range of loading conditions. After control recordings were taken at \(P_{LV,VED} \approx 7\) mmHg, \(P_{LV,VED}\) was increased in \(-5\) to \(-27\) mmHg with measurements taken while the ventilator was turned off at end expiration for 30 s. These measurements included \(P_{LA}, P_{AO}, P_{PV}, P_{Peri},\) aortic flow (\(Q_{AO}\)), PV flow (\(Q_{PV}\)), LA and LV dimensions, and Doppler flow velocity at the mitral valve. The animals were given enough time to recover hemodynamically between each incremental load. At the end of the experiment, while deeply anesthetized, the dogs were euthanized by an intracardiac injection of KCl.

**Data analysis.** The beginning of LA systole (i.e., the A wave) was defined by the rapid increase in \(P_{LA}\) (or \(P_{LV}\)) values before the abrupt rise in \(P_{LV}\). \(P_{LA}\) was assumed to be a function of the product of the dimensions: \(P_{LA} = k_{LV} \cdot D_L \cdot D_T\), analogous to \(P_{LV} = k_{LV} \cdot V_{LA}\), \(k_{LV}\) and \(k_{LV}\) were determined as described below. Pressure-volume work (\(W_{P-V}\)), defined as total work produced by the LA during atrial systole, was calculated by integrating the area described by the LA transmural P-V loop during atrial systole, where \(P_{LA,Tm} = P_{LA} - P_{Peri}\). LV stiffness was calculated as \(\Delta P_{LV}/\Delta V_{LV}\), where \(\Delta P_{LV}\) was the difference in \(P_{LV}\) from minimum LV diastolic pressure to the pre-A-wave pressure and \(\Delta V_{LV}\) was the corresponding change in \(V_{LV}\).

We accepted the accuracy of stroke volume (SV) measured by the aortic flow probe and scaled mitral and PV flows and \(V_{LA}\) and \(V_{LV}\) accordingly, assuming a momentary steady state and that the measured PV flow was representative of total inflow to the LA. Over one cardiac cycle, aortic stroke volume was calculated by integrating aortic flow (\(Q_{Ao}\)) with respect to time: \(SV = \int Q_{Ao} dt\). During ejection, the \(D_{AP} \cdot D_{B-A} \cdot D_{S-F}\) product was plotted vs. \(\int Q_{Ao} dt\); the slope of this relation was found by linear regression and set equal to \(k_{LV}\). Thus \(SV = \Delta V_{mitral} = A_{mitral} \cdot \int U_{mitral} dt\), where \(A_{mitral}\) is the average area of the mitral orifice and \(U_{mitral}\) is the mitral velocity determined from Doppler echocardiography. Total PV flow (\(Q_{PV}\)) during a cardiac cycle was also set equal to aortic stroke volume: \(SV = \Delta V_{LA} = k_{PV} \cdot \int Q_{PV} dt\), where \(Q_{PV}\) was determined by flowmeter. Finally, the change in LA volume (\(\Delta V_{LA}\)) was set equal to the instantaneous difference between the integrals of LA inflow and outflow: thus \(\Delta V_{LA} = k_{PV} \cdot \int Q_{PV} dt\).

Hydraulic work (\(W_h\)) was defined as the LA pump work, the time-integral of pressure and flow. Therefore, forward hydraulic work is the work done to move blood forward through the mitral valve during atrial systole: \(W_{h-Tm} = A_{mitral} \cdot \int P_{LA} \cdot U_{mitral} dt\). Backward hydraulic work is the work done to move blood retrogradely into the PVs during atrial systole: \(W_{h-PV} = k_{PV} \cdot \int P_{PV} \cdot Q_{PV} dt\). The total

### Table 1. Hemodynamic data at \(P_{LV,VED} = 8, 16,\) and \(24\) mmHg

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value 1 (SD)</th>
<th>Value 2 (SD)</th>
<th>Value 3 (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, beats/min</td>
<td>56.6 ± 2.8</td>
<td>67.5 ± 2.3</td>
<td>74.4 ± 4.4</td>
</tr>
<tr>
<td>Cardiac output, l/min</td>
<td>1.67 ± 0.22</td>
<td>2.32 ± 0.12</td>
<td>2.71 ± 0.36</td>
</tr>
<tr>
<td>Stroke volume, ml/beat</td>
<td>28.3 ± 7.1</td>
<td>33.7 ± 8.8</td>
<td>36.4 ± 5.2</td>
</tr>
<tr>
<td>Arterial pressure, mmHg</td>
<td>118 ± 6/74 ± 9</td>
<td>142 ± 8/77 ± 9</td>
<td>126 ± 12/90 ± 10</td>
</tr>
<tr>
<td>P_{LV} pre-A-wave, mmHg</td>
<td>6.6 ± 1.5</td>
<td>13.2 ± 1.6</td>
<td>20.7 ± 0.9</td>
</tr>
<tr>
<td>P_{LV,VED}, mmHg</td>
<td>8.3 ± 1.1</td>
<td>16.3 ± 1.3</td>
<td>23.9 ± 0.7</td>
</tr>
<tr>
<td>P_{LA}, mmHg</td>
<td>7.7 ± 0.9</td>
<td>14.1 ± 1.6</td>
<td>22.5 ± 1.6</td>
</tr>
<tr>
<td>P_{PV}, mmHg</td>
<td>7.3 ± 1.5</td>
<td>14.5 ± 1.7</td>
<td>22.6 ± 1.6</td>
</tr>
<tr>
<td>P_{Peri}, mmHg</td>
<td>4.8 ± 1.5</td>
<td>9.7 ± 2.7</td>
<td>13.9 ± 4.4</td>
</tr>
</tbody>
</table>

Values are means (SD); \(n = 6\). End-diastolic left ventricle pressure (\(P_{LV,VED}\)), left atrial pressure (\(P_{LA}\)), pulmonary venous pressure (\(P_{PV}\)), and pericardial pressure (\(P_{Peri}\)) were measured at LV end diastole.
hydraulic work produced by LA contraction is the sum of the forward and backward hydraulic work: \( W_H = W_{H\text{-mitral}} + W_{H\text{-PV}} \).

The intensity of a forward-going wave (\( dI_{W+} \)) is equal to \( (pc/4)\cdot(dP + pcdU)^2 \), and the intensity of a backward-going wave (\( dI_{W-} \)) is equal to \( -(pc/4)\cdot(dP - pcdU)^2 \), where \( p \) is the density of the blood, \( c \) is the wave speed, and \( dU \) is the incremental change in velocity during a sampling interval (~5 ms), measured by Doppler echocardiography for the mitral orifice and by flowmeter for the PV (\( Q_{PV} = U_{PV}\cdot A_{PV} \), where \( A_{PV} \) was estimated from the size of the flow probe). Wave speed was calculated using the equation \( c = dP/dU \) at the beginning of atrial systole, when a compression wave is present and reflections from previous wave activity were assumed to be minimal. The net intensity (\( dIW = dI_{W+} + dI_{W-} \)) is the (instantaneous) sum of the intensities of the forward (\( dI_{W+} \)) and backward-going (\( dI_{W-} \)) wave and therefore is equal to \( (dP/dU)^2 \) (43). It measures the combined wave effects at that instant and location and thus indicates whether the forward or backward wave is dominant at a given instant. The time integral of intensity is the energy (\( IW \)) carried by a wave. Because \( W_{IA} \) is a time-domain analysis, waves can be temporarily related to changes in hemodynamic parameters (34).

The reflection coefficient at the mitral valve was calculated by dividing the energy of the (reflected) backward compression wave by the energy of the (incident) forward compression wave generated by LA contraction (\( kW_{W-}/kW_{W+} \)). Linear regressions were performed, and pooled data are expressed as means (SD).

### RESULTS

Hemodynamic data recorded under control conditions are shown in Table 1. Figure 1A shows the relations between intracavitary and transmural LA pre-A-wave pressure (\( P_{LA} \) and \( P_{LA-Tm} \), respectively) and normalized LA volume (\( V_{LA} \); percent control) for each dog. Figure 1B shows the relations between \( P_{LA} \) and \( P_{LA-Tm} \) and \( V_{LA} \) for the pooled data. The regressions of the pooled data indicate that increasing \( V_{LA} \) by 50% was associated with an increase in \( P_{LA} \) from 8.9 to 19.1 mmHg; however, \( P_{LA-Tm} \) only increased from 3.1 to 5.6 mmHg. The difference between intracavitary and transmural pressure is due to pericardial constraint.

Normalized \( P_{LA-Tm-V} \) work (\( W_{P-V} \); percent control) and normalized pre-A-wave volume \( V_{LA} \) were found to be directly, quasi-linearly correlated (data not shown), demonstrating the Frank-Starling relation. Figure 2 shows the relations between normalized \( W_{P-V} \) and, as alternative measures of LA preload, pre-A-wave \( P_{LA} \) and \( P_{LA-Tm} \) (pooled data).

Figure 3, A and B, shows transmitral forward volume (A-wave volume) and retrograde volume into the PVs (Ar-wave volume), respectively derived from integrated A-wave velocities and PV flows, plotted vs. \( P_{LVED} \). At higher values of \( P_{LVED} \), Ar-wave volume decreased and A-wave volume increased. The ratio of retrograde-to-forward volume (Ar/A-wave volume) vs. \( P_{LVED} \) is shown in Fig. 4. Since the time courses of the two waves are similar, this plot implies that retrograde flow (A wave) increases at a greater rate than forward flow (A wave) as \( P_{LVED} \) increases. The difference in the duration of the Ar wave and the A wave (Ard - Ad) also increased with increasing \( P_{LVED} \), as shown in Fig. 5A. Consistent with previous investigations, if \( P_{LVED} \) exceeded 13.7 mmHg, the duration of the Ar wave exceeded that of the A wave (30).

The data shown in Fig. 4 suggest that the relation between the durations of the A and Ar waves and \( P_{LVED} \) (Fig. 5A) might be paralleled by a relation between the ratio of A- and Ar-wave volumes and \( P_{LVED} \). Accordingly, the data shown in Fig. 4 were pooled and correlated (see Fig. 5B). (Two outliers, the
ratios of $\sim 0.4$ in dogs 3 and 5, were arbitrarily excluded.) Note that the volume ratio is $0.1$ when PLVED $= 15 \text{ mmHg}$.

Figure 6 shows representative hemodynamic measurements during LA contraction and WIA of transmitral flow velocity and PV flow. As the LA begins to contract (indicated by the increase in $U_{mitral}$ and $P_{LA}$ in Fig. 6A; note vertical line), it generates a compression wave that travels both forward, into the LV (Fig. 6C), and backward, into the PVs (Fig. 6D). The backward-going compression wave decelerates the antegrade PV flow (indicated by diminishing $Q_{PV}$, Fig. 6B) and increases $P_{PV}$, whereas the forward-going compression wave accelerates blood into the LV and is partially reflected, generating a backward compression wave at the mitral orifice (Fig. 6C). The reflected backward compression wave is transmitted from the LV across the LA to the PVs and appears to augment the backward compression wave seen in the PVs (Fig. 6D, second peak; note dashed slanting line). Net intensity ($d_{W}$), the (instantaneous) sum of the intensities of the forward ($d_{W^+}$) and backward-going waves ($d_{W^-}$), is a measure of the combined wave effects at that instant and location.

If wave energy (i.e., the time-integral of intensity) is a measure of the work applied to accelerate or decelerate the blood, hydraulic work ($W_{H}$) should depend on net wave energy ($I_{W}$). Accordingly, we plotted the A-wave $W_{H}$ vs. mitral $I_{W}$ (Fig. 7A) and the Ar-wave $W_{H}$ vs. PV $I_{W}$ (Fig. 7B). For each dog, $W_{H}$ was linearly related to $I_{W}$ ($r^2$ ranged from 0.79 to 0.98 in Fig. 7A and from 0.94 to 0.99 in Fig. 7B). Slopes were on the order of 100, implying that $I_{W}$ is $\sim 1\%$ of total $W_{H}$.

Figure 8 shows that LV stiffness was proportional to pre-A-wave $P_{LV}$. Acute volume loading results in an increase in the operative stiffness of the chamber, consistent with a curvilinear diastolic P-V relation. We do not suggest that the diastolic P-V relationship is shifted upward, which would indicate a change in the intrinsic structure of the muscle or increase in external constraint. Figure 9 demonstrates that the reflection coefficient (i.e., the energy of the reflected wave divided by the energy of the incident wave, $I_{W^-}/I_{W^+}$) was proportional to LV stiffness. The relations were linear for each dog ($r^2$ ranged from 0.64 to 0.94).

Figure 10 shows Ar-wave volume plotted vs. the energy of the reflected mitral wave ($I_{W^-}$), indicating that backward flow into the PVs is directly related to the net energy of the reflected wave ($r^2$ ranged from 0.63 to 0.98).

**DISCUSSION**

In the present study of the dynamics of LA systole in normal anesthetized dogs, we used WIA to assess forward flow through the mitral valve and backward flow into the pulmonary veins. This technique allowed us to quantitatively assess the mechanisms responsible for changes in forward and backward flow at different LV filling pressures. Our results are consistent with what has been observed by others in that, at elevated PLVED during volume loading, forward flow was reduced and retrograde flow into the pulmonary veins increased. However, WIA also showed that increased operative LV stiffness increases the reflection coefficient so that a greater proportion of the incident forward compression wave generated by LA con-

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Fig. 4. Ratio of Ar-wave volume to A-wave volume vs. $P_{LV}$. These data imply that retrograde flow increases faster than forward flow as $P_{LV}$ increases.

Fig. 5. A: difference between the duration of the Ar wave and the duration of the A wave (Ard - Ad) vs. $P_{LV}$ [(Ard - Ad) = 0.004$P_{LV}$ - 0.06 ($r^2$ = 0.55)]. When $P_{LV}$ exceeded 13.7 mmHg, the duration of the Ar wave exceeded that of the A wave. B: ratio of Ar-wave volume to A-wave volume vs. $P_{LV}$; the data shown in Fig. 4 were pooled and correlated. (Two outliers, the ratios of 0.4 in dogs 3 and 5, were arbitrarily excluded.) [(Ar-wave volume/A-wave volume) = 0.006$P_{LV}$ - 0.02 ($r^2$ = 0.25)]. Note that the volume ratio is 0.1 when $P_{LV}$ = 15 mmHg.
traction is reflected back toward the LA. This backward compression wave diminishes forward flow into the LV and increases retrograde flow through the PVs. Thus WIA helped to clarify the mechanisms underlying the previously described clinical observations.

**LA mechanics and the pericardium.** As our group has shown previously for the LV (3, 28), LA transmural pressure increases during volume loading, but much less than LA intracavitary pressure (Fig. 1). Also, LA transmural pressure is a better measure of LA preload, in that the relationship between LA work and transmural pressure is more coherent than that with intracavitary pressure (Fig. 2).

**Duration of A and Ar waves.** The inverse relationship among elevated \( P_{\text{LVED}} \), decreased transmitral A wave flow, and augmented PV retrograde flow has been well established (2, 15, 30) such that LV diastolic function can be assessed clinically by measuring the Ar wave velocity and Ard-Ad wave duration difference as an indicator of increased \( P_{\text{LVED}} \) (1, 8, 14, 25, 37, 38, 45). In 1993, Rossvoll and Hatle (38) showed that a positive Ard-Ad difference predicts a \( P_{\text{LVED}} \) in excess of 15 mmHg. Greenberg et al. (16) explained the diminished atrial contribution to LV filling with elevated \( P_{\text{LVED}} \) by the curvilinear nature of the LV diastolic P-V relation. As \( P_{\text{LVED}} \) increases, the slope of the LV P-V curve (i.e., LV stiffness) increases such that a given LA contraction will increase LV pressure more and increase LV volume less (27). Rossvoll and Hatle (38) further suggested that increased LV stiffness contributes to augmenting PV retrograde flow by rapidly elevating \( P_{\text{LA}} \) during atrial contraction. Our results are in accordance with accepted theories such that elevated LV stiffness due to volume loading (Fig. 8) results in diminished A volume and

Fig. 6. Wave intensity analysis of LA contraction. 

A: LV \( (P_{\text{LV}}) \) and LA \( (P_{\text{LA}}) \) pressures and mitral velocity \( (U_{\text{mitral}}) \). B: pulmonary venous pressure \( (P_{\text{PV}}) \) and flow \( (Q_{\text{PV}}) \). C: intensity of forward \( (d_{W^+}) \); light solid line above zero)- and backward-going waves \( (d_{W^-}; \text{dashed line below zero}) \) and net intensity \( (d_W; \text{thick solid line}) \) at the mitral valve. D: intensity of forward \( (d_{W^+}; \text{light solid line above zero}) \)- and backward-going waves \( (d_{W^-}; \text{dashed line below zero}) \) and net intensity \( (d_W; \text{thick solid line}) \) in a pulmonary vein (PV). At the beginning of its contraction, the LA generates a forward-going compression wave (FCW) through the mitral valve that is partially reflected (BCW; C). It also generates a backward-going compression wave (BCW) into the orifice of the pulmonary vein (D). Note that the BCW in C appears to account for the second peak in the BCW in D, which occurs after a delay consistent with propagation across the LA.

Fig. 7. A: A-wave hydraulic work vs. the net energy of the forward wave \( (I_W) \) at the mitral valve. B: Ar-wave hydraulic work vs. the net energy of the backward wave \( (I_W) \) at the orifice of the PV. For both the mitral valve and the PV, net wave energy predicts hydraulic work. For color code, see Fig. 4.
augmented Ar volume (Fig. 3, A and B). As well, Fig. 5 shows that a positive Ard-Ad difference occurs at PLVED above ~14 mmHg. However, our results clarify the mechanisms involved by demonstrating the effects of reflected waves from the LV on forward transmitral flow and retrograde flow into the PVs. In particular, they suggest that the A- to Ar-wave volume ratio is approximately proportional to PLVED; approximately one-tenth the forward volume goes backward when PLVED = 15 mmHg and two-tenths, when PLVED = 30 mmHg (see Fig. 5B).

Wave reflection. The potential for wave reflection to have a negative effect on forward flow through the mitral valve and positive effect on backward flow into the pulmonary veins has not been studied previously. We demonstrate presently that as the LV becomes stiffer by moving along its P-V curve, the reflection coefficient (i.e., the fraction of the energy of the forward incident wave generated by the contracting LA that is reflected backward from the LV) is increased from negligible values at low diastolic pressures to ~0.4. The nature of a reflected wave (i.e., compression or expansion) and the ratio of the reflected to the incident wave depend on the reflection site (34). Therefore, although both IW+ and IW− increase with PLVED, as the LV (reflection site) became stiffer, the increase in IW− was greater than the increase in IW+ (Fig. 9). Since wave energy is additive (i.e., IW = IW+ + IW−), the energy of the (reflected) backward compression wave partially negates the energy of the forward compression wave. WIA quantifies the energy needed to overcome inerterance and accelerate blood (16). When LV stiffness increases, the (reflected) backward compression wave increasingly negates the effect of the (incident) forward compression wave, limiting the acceleration of blood through the mitral valve (i.e., decelerating the forward flow of blood).

We further suggest that the (reflected) backward compression wave is transmitted across the LA to the PV and acts to augment PV retrograde flow (i.e., the Ar wave). This is consistent with the conclusions of Dernellis and Panaretou (9), who demonstrated that LA input impedance (frequency-dependent pressure-flow ratios, a measure of the opposition to blood flow from the PV to the LA) and peak PV Ar flow were increased in hypertensive patients compared with controls. They commented that LA input impedance is dependent on the downstream circulation (e.g., the LV), in accordance with our finding that increased LV stiffness augments the (reflected) backward compression wave and PV Ar flow. Our findings also are consistent with those of Hellevik et al. (18), who demonstrated with a mathematical model that all propagated or reflected waves in the PVs originate in the left heart.

LA work directed forward through the mitral valve (i.e., forward hydraulic work) and work directed backward through the PV (i.e., backward hydraulic work; the respective integrals of the products of PLA and QA and of PPV and QAr) include the energy spent to overcome inerterance, the energy used to overcome viscous losses, and the energy expended against elastance. Similar to LV systole, which was described by Rushmer (39) as causing an “initial ventricular impulse,” the impulse generated by the LA during systole produces a forward compression wave through the mitral valve and a backward compression wave through the PV. The impulse that accelerates QA was quantified as the energy under the forward compression wave.
wave at the mitral valve (Fig. 6C) and the impulse that accelerates \( Q_{Ar} \) was quantified as the energy under (or above, because the wave is plotted negatively) the backward compression wave at the PV (Fig. 6D).

As shown in Fig. 7, the hydraulic work propelling blood through a specific site is proportional to the net wave energy at that site. Therefore, as LV stiffness increases, the backward compression wave increasingly negates the effect of the forward compression wave and contributes, at least in part, to the decline in transmitral hydraulic work (forward flow). It is also noteworthy that the Ar volume propelled backward into the PVs is proportional to the energy of the reflected wave (Fig. 10). We suggest that the reflected backward compression wave augments the effect of the primary PV backward compression wave (generated directly by LA contraction), accelerating blood in the retrograde direction and increasing backward hydraulic work. Thus increased LV stiffness limits forward flow during atrial systole by generating a backward-going compression wave that also augments retrograde flow into the pulmonary veins.

With respect to both mitral and PV flow, hydraulic work is proportional to wave energy, the magnitude of this proportionality being on the order of 100 to 1 (Fig. 7). This value is consistent with unpublished data from this laboratory and the comment by Jones and Sugawara (21) that wave intensity represents only a small proportion of the total power generated.

**LA work.** Since the atrial contribution to LV filling is reduced during volume loading (22, 25) and in advanced forms of heart failure (23), the LA may perform poorly when \( P_{LV} \) is elevated. Although this is true in end-stage heart failure, when the progressive decrease in LA work may be related directly to failure of atrial muscle (4), we have shown that total LA work and the sum of the forward and backward hydraulic work actually increase with increasing levels of \( P_{LV} \) (Fig. 2). We have found that the Frank-Starling mechanism governs LA performance: P-V work increased in proportion to pre-A-wave \( V_{LA} \), which in turn was proportional to transmural pressure (16, 19–22, 36, 39). The decrease in forward flow was associated with increased retrograde flow (Fig. 3) such that the total volume and work associated with LA contraction continued to increase with increased \( P_{LV} \). This is consistent with previous work that showed an initial increase in LA pump function associated with elevated LV stiffness in mild heart failure (10). As demonstrated by Hoit et al. (20) in an open-pericardium model, both LA work and stroke volume increase in volume-loaded conditions; however, the efficiency of the LA appears to decrease as the fraction of forward or effective output decreases (10, 20, 23). These results might seem to contradict clinical experience, given that patients with stiff ventricles (e.g., hypertension, and hypertrophic cardiomyopathy) might not tolerate well the loss of the atrial contribution to LV filling. However, these observations in acute experiments merely indicate that the normal LA is less efficient when LV stiffness is increased. With compensatory LA hypertrophy and dilatation, even if some of the LA output is directed backward, forward output clearly is still beneficial and may be critical to LV performance.

**Limitations.** These acute experiments were performed in anesthetized, open-chest dogs that had been extensively instrumented. As well, short-term volume loading may not be representative of the changes that occur in chronic pathological conditions such as structural remodeling of the heart wall. Thus it would be desirable for more physiological experiments and clinical studies to be designed to confirm our results and conclusions.

As discussed in previous studies (29, 42, 44), there are limitations in applying one-dimensional WIA to the complex three-dimensional geometry of the LV. However, we assume that the quasi-cylindrical mitral orifice can be considered to be a one-dimensional system, regardless of the possible complexity of wave motion in the LV cavity.

Although the mitral valve area decreases during the course of the Doppler E wave (5), it was not possible to take this into account, and instead, we calculated an average value based on the relation of the integrals of the E and A waves to the LV stroke volume. As well, we were not able to account for possible changes in cross-sectional area. Bowman and Kovacs (6) suggested that effective PV area varies throughout the cardiac cycle and becomes smaller during late diastole, which would tend to minimize retrograde flow and help preserve antegrade flow. Comparing the flow patterns in different PVs, they also concluded that peak flows were not reached simultaneously (6, 7, 13). Thus our assumption that the flow in a single PV was representative of total LA inflow may not be entirely accurate.

Finally, there is no gold standard for calculating LA volume due to the complex shape of the chamber. In the present study, LA volume was calculated with sonomicrometry using a modified ellipsoid shape, \( \Delta V_{LA} = k_{LA} \cdot DL \cdot DR \), and was then scaled according to \( \Delta V_{LA} \) calculated from LA outflow minus inflow. This method does not consider the volume of the atrial appendage; however, we found that appendage dimension and shortening depended on transmural pressure in the same way that was true of the LA (data not shown).

In conclusion, using WIA analysis, we were able to show that as LV stiffness was increased acutely, the reflected backward compression wave also increased. This larger reflected wave partially negated the effect of the forward compression wave in propelling blood forward through the mitral valve and augmented the backward compression wave propelling blood back through the pulmonary veins. Thus, despite increased LA work, forward hydraulic work and flow were reduced and backward hydraulic work and flow were increased. These results explain, at least in part, the changes that occur to the transmitral A wave and pulmonary venous Ar wave with increased LV stiffness.

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**REFERENCES**

