Effect of Chronic Pressure Overload on the Maximal Rate of Pressure Fall of the Right Ventricle*

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The maximal rate of fall in the right ventricular pressure (negative dp/dt) was evaluated in 34 patients. Eight had normal pulmonary arterial pressure. Seventeen had pulmonary arterial hypertension, and nine had pulmonary arterial hypertension with right ventricular failure. The right ventricular maximal negative dp/dt in patients with normal pulmonary arterial pressure was 170 ± 20 mm Hg/sec. In patients with pulmonary arterial hypertension not accompanied by right ventricular failure, this value was 670 ± 60 mm Hg/sec; and in patients with right ventricular failure, it was also 670 ± 60 mm Hg/sec. This was higher than in control subjects (P < 0.001). The maximal positive dp/dt was also higher in patients with pulmonary hypertension, regardless of the presence of right ventricular failure. Right ventricular maximal negative dp/dt correlated with right ventricular maximal positive dp/dt (r = 0.72). Right ventricular maximal negative dp/dt in patients who were not in right ventricular failure correlated linearly with pulmonary arterial systolic pressure (r = 0.83) and pulmonary arterial diastolic pressure (r = 0.83). At any level of pulmonary arterial systolic pressure, right ventricular maximal negative dp/dt in patients with right ventricular failure was lower than in patients with the same level of pulmonary arterial hypertension who were not in failure. These observations indicate that right ventricular maximal negative dp/dt is dependent on load. Even in the presence of right ventricular failure, right ventricular maximal negative dp/dt exceeded values in control subjects.

Contraction and relaxation of the ventricles are interdependent and related functions. Therefore, a comprehensive understanding of the contractile behavior of the ventricles requires a description of the course of myocardial relaxation over time. This is of special importance, since dissimilar changes in contraction and relaxation have been reported in isolated cardiac muscle and in the intact heart. In the left ventricle, heart failure, hypoxia, and ischemia prolong isovolumic relaxation; while isoproterenol, calcium, and phenylephrine have dissimilar effects upon the rate of rise and the rate of fall of left ventricular pressure.

Although several investigators have described the characteristics of relaxation of isolated muscular segments and the intact left ventricle in animals and patients, the characteristics of relaxation of the right ventricle have been sparsely evaluated. In view of the role of the diastolic properties of the ventricle in maintaining satisfactory ventricular performance, we performed this study of the maximal rate of the fall of pressure (negative dp/dt) in the right ventricle in patients with normal pulmonary arterial pressure and in patients with a chronic pressure overload of the right ventricle.

**Materials and Methods**

Maximal negative dp/dt in the right ventricle was investigated in 34 patients during diagnostic cardiac catheterization. Eight had normal pulmonary arterial pressure, 17 had pulmonary hypertension without right ventricular failure, and nine had pulmonary hypertension with right ventricular failure.

Patients were categorized as having a normal pulmonary arterial pressure if it did not exceed 30/12 mm Hg. In view of the fact that right ventricular function has been shown to be affected by decreased myocardial perfusion, all patients with right coronary or left circumflex coronary arterial stenosis were excluded from the control group. One patient with stenosis of the left anterior descending coronary artery was admitted to the control group because the stenosis was distal to the second diagonal branch and was thought not to affect right ventricular perfusion.

Right ventricular failure was defined as the presence of hepatomegaly, ascites, or dependent edema in patients with an elevated right atrial pressure (more than 9 mm Hg). Thus, the diagnosis of right ventricular failure was essentially a clinical diagnosis, although measured pressures were

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substituted for the physical sign of systemic venous hypertension.

Patients were excluded if they had tricuspid regurgitation, as indicated by a systolic murmur recorded within the right atrium or prominent right atrial v waves. Patients were also excluded if they had an intracardiac shunt. Since “emphysema heart” may differ from pulmonary hypertensive heart disease, partially due to polycythemia and hypoxemia, 30 patients were excluded if they had clinical evidence of chronic obstructive pulmonary disease. The level of hemoglobin in control subjects, patients with pulmonary hypertension, and patients with pulmonary hypertension and right ventricular failure was 14.5 ± 0.8 gm/100 ml, 13.5 ± 0.5 gm/100 ml, and 13.5 ± 0.7 gm/100 ml, respectively. The systemic arterial oxygen saturation of patients with pulmonary hypertension was 96 ± 1 percent and in those with pulmonary hypertension and right ventricular failure was 96 ± 2 percent.

Of the eight control subjects, six had no heart disease, one had a healed left ventricular stab wound, and one had mild aortic insufficiency. Cardiac diagnoses in the 17 patients with pulmonary hypertension included the following: coronary heart disease, 5; mitral valvular disease, 9; aortic valvular disease, 1; cardiomyopathy, 1; and undetermined cause, 1. Of the nine patients with pulmonary hypertension with right ventricular failure, four had coronary heart disease, two had mitral valvular disease, two had cardiomyopathy, and in one the cause was undetermined.

 Patients with pulmonary hypertension (54 ± 3 years), and those with pulmonary hypertension and right ventricular failure (55 ± 3 years) were older than the control subjects (41 ± 4 years). None of the patients in the control group received propranolol or digitals, although two were treated with diuretic drugs. Two patients with pulmonary hypertension were treated with propranolol. Twelve of the patients with pulmonary hypertension and all of the patients with right ventricular failure were treated with digitals. Eleven of the patients with pulmonary hypertension and all of the patients with right ventricular failure were treated with diuretic drugs.

None of the patients had electrocardiographic evidence of right ventricular hypertrophy. P pulmonale was present in one patient with pulmonary hypertension. Complete right bundle-branch block was present in two patients with right ventricular failure, and right axis deviation was present in one patient with right ventricular failure. The criteria that we selected for making electrocardiographic interpretation have been previously described.

All pressures were measured with catheter-tip micromanometers (Millar Instruments, Inc.). Although the frequency response of the pressure sensor was essentially flat within ±2 percent at 5 kHz and ±5 percent at 10 kHz, pressures were filtered using a 250 Hz low pass filter. The frequency response of the recorder (Electronics for Medicine VR-6) was flat to 700 Hz. All measurements of pressure were made at paper speeds of 200 mm/sec. Sound was recorded internally from the same catheter-tip micromanometer used for recording pressure.

Maximal negative dp/dt and maximal positive dp/dt were calculated with the use of a computer (Hewlett-Packard 21 MX) and an electronic digitizer (Numonics) at 1-mm (5-msec) or 0.25-mm (1.55-msec) intervals. Instantaneous values of dp/dt and negative dp/dt were obtained by curve-fitting the appropriate portions of the right ventricular pressure curve using a fifth-order polynomial. The techniques for measuring positive dp/dt using this method have been described in detail. The portion of right ventricular pressure that was curve-fitted for the evaluation of isovolumic contraction was measured from the point of right ventricular end-diastolic pressure to the level of pulmonary arterial diastolic pressure. For the evaluation of negative dp/dt, right ventricular pressure was curve-fitted from the beginning of the high-frequency components of the simultaneously recorded pulmonary component of the second sound to the lowest portion of the right ventricular pressure curve. The curve-fitted values of pressure during isovolumic contraction and isovolumic relaxation were within 3 percent of actual measured values at each point along the curve. The average value of measurements of three beats was reported.

Results

Examples of right ventricular pressure in a patient with normal pulmonary arterial pressure and a patient with pulmonary hypertension accompanied by right ventricular failure are shown in Figures 1 and 2. The maximal right ventricular negative dp/dt in patients with pulmonary hypertension who were not in right ventricular failure was 670 ± 60 mm Hg/sec (mean ± SE), and this value was also 670 ± 60 mm Hg/sec in patients with right ventricular failure. This was significantly higher than in control subjects (170 ± 20 mm Hg/sec) (P < 0.001) (unpaired t-test) (Fig 3).

The maximal right ventricular negative dp/dt in normotensive patients and patients with pulmonary

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Table 1——Central Hemodynamic Measurements*  

<table>
<thead>
<tr>
<th>Data</th>
<th>Pulmonary Hypertension</th>
<th>No Congestive Heart Failure</th>
<th>Congestive Heart Failure</th>
</tr>
</thead>
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<tr>
<td></td>
<td>Control Subjects</td>
<td>Mean ± S.E.</td>
<td>Mean ± S.E.</td>
</tr>
<tr>
<td>Pressure, mm Hg</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Pulmonary artery mean</td>
<td>18/7 ± 1/1</td>
<td>50/25 ± 5/2</td>
<td>70/38 ± 5/2</td>
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<tr>
<td>Right ventricular end-diastolic mean</td>
<td>2 ± 0.3</td>
<td>3 ± 4</td>
<td>13 ± 1†</td>
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<tr>
<td>Right ventricular mean</td>
<td>4 ± 1</td>
<td>4 ± 1</td>
<td>14 ± 2</td>
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<tr>
<td>Heart rate, beats per min</td>
<td>83 ± 6</td>
<td>87 ± 4</td>
<td>91 ± 4</td>
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<td>Cardiac index, L/min/sq m</td>
<td>2.9 ± 0.2</td>
<td>2.1 ± 0.2†</td>
<td>1.5 ± 0.1†</td>
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<td>Stroke index, ml/stroke/sq m</td>
<td>38 ± 3</td>
<td>24 ± 2**</td>
<td>18 ± 1†</td>
</tr>
<tr>
<td>Pulmonary vascular resistance, dyne sec cm–4</td>
<td>53 ± 7</td>
<td>310 ± 60†</td>
<td>510 ± 40†</td>
</tr>
<tr>
<td>Right ventricular work, kg-m/min/sq m</td>
<td>0.40 ± 0.07</td>
<td>0.94 ± 0.12†</td>
<td>0.91 ± 0.05†</td>
</tr>
</tbody>
</table>

*Table values are means ± S.E.

**P < 0.01, compared to control value.
†P < 0.001, compared to control value.
‡P < 0.02, compared to control value.
Pressure in pulmonary artery (PA) and right ventricle (RV) sound recorded in pulmonary artery of patient with normal right-sided pressures.

Pressure in pulmonary artery (PA) and right ventricle (RV), sound in pulmonary artery, and ECG in patient with pulmonary hypertension and right ventricular failure.

hypertension who were not in right ventricular failure correlated linearly with pulmonary arterial systolic pressure ($r = 0.83$) (Fig 4) and pulmonary arterial diastolic pressure ($r = 0.83$). At any level of pulmonary arterial systolic or diastolic pressure, the maximal negative dp/dt of patients with right ventricular failure in general was lower than in patients with the same level of pulmonary hypertension who were not in failure (Fig 4).

In patients with normal pulmonary arterial pressure, the positive dp/dt was $200 \pm 20$ mm Hg/sec. In patients with pulmonary hypertension the maximal positive dp/dt, $500 \pm 30$ mm Hg/sec, was higher ($P < 0.001$). In patients with right ventricular failure, this value was $610 \pm 70$ mm Hg/sec, which was also higher than in patients with normal pulmonary arterial pressure ($P < 0.001$). Right

Figure 3. Right ventricular maximal negative dp/dt (RV MAX NEG DP/DT) in control subjects (C), patients with pulmonary hypertension (PA-HTN), and patients with pulmonary hypertension accompanied by right ventricular failure (PA-HTN CHF). Probabilities refer to comparisons with control subjects.

Figure 4. Relation of right ventricular maximal negative dp/dt (RV MAX NEG DP/DT) to pulmonary arterial (PA) systolic pressure. Regression line and correlation coefficient (R) apply only to patients without right ventricular failure (NO CHF). Solid circles indicate patients without right ventricular failure; open circles indicate patients with right ventricular failure.
ventricular maximal negative dp/dt correlated linearly with maximal positive dp/dt ($r = 0.72$).

**Discussion**

In the evaluation of the characteristics of isovolumic relaxation of the left ventricle, two indices have been recommended. One is maximal negative dp/dt; the other is the time constant, T, of the semilogarithmic fall of ventricular pressure following maximal negative dp/dt. The time constant, T, has been considered more indicative of the mechanical properties of the left ventricle during isovolumic relaxation because it is less dependent upon systolic stress and the end-systolic length of fibers than maximal negative dp/dt. It has been stated that maximal negative dp/dt reflects only one instant of isovolumic relaxation, whereas T reflects a larger portion of isovolumic relaxation, from the time of maximal negative dp/dt to the time when the left ventricular pressure reaches the diastolic level.

We attempted to calculate T in the right ventricle of the patients in this study using methods described for the left ventricle; however, in patients with normal pulmonary arterial pressure, maximal negative dp/dt occurred late on the downstroke of ventricular pressure (Fig 1). Therefore, the time constant, T, for the right ventricle would have reflected a very small fraction of the isovolumic period in some patients. In some patients the defined interval for the evaluation of T was absent because maximal negative dp/dt occurred at the end of isovolumic relaxation. Therefore, the time constant, T, as defined for the left ventricle, was not measurable in the right ventricle of patients with normal pulmonary arterial pressure.

Since an accurate assessment of the time constant, T, was not possible in the normotensive right ventricle, the rate of isovolumic relaxation of the right ventricle was evaluated on the basis of maximal negative dp/dt. Maximal negative dp/dt was shown to be dependent on load. For a given level of pulmonary hypertension, maximal negative dp/dt was somewhat lower in patients with right ventricular failure, in comparison to patients with pulmonary hypertension who were not in failure; however, even in patients with failure, maximal right ventricular negative dp/dt as well as positive dp/dt exceeded values in normotensive patients. Maximal right ventricular negative dp/dt correlated with maximal positive dp/dt. These observations suggest that the increased load imposed upon the right ventricle by pulmonary hypertension results in a greater contractile effort manifested by a more rapid maximal rate of fall in pressure during isovolumic relaxation, as well as a greater maximal rate of rise in pressure during isovolumic contraction.

The observed dependence on load of the maximal right ventricular negative dp/dt was comparable to the behavior of left ventricular maximal negative dp/dt. Similarly, a correlation in the left ventricle of maximal negative dp/dt with left ventricular maximal positive dp/dt has also been observed, just as we observed a correlation in the right ventricle of maximal negative dp/dt with right ventricular maximal positive dp/dt; however, in regard to the presence of right ventricular failure, maximal right ventricular negative dp/dt behaved in a strikingly different fashion from left ventricular negative dp/dt in patients with left ventricular failure. In patients with left ventricular failure, left ventricular maximal negative dp/dt was lower than in patients with normal left ventricular performance; whereas in patients with right ventricular failure, the maximal right ventricular negative dp/dt exceeded values in control subjects.

The apparent difference in behavior of right ventricular and left ventricular negative dp/dt perhaps can be explained on the basis of differences in the mechanism of right ventricular and left ventricular failure. In patients with left ventricular failure, isovolumic contraction and relaxation are impaired due to damage of the left ventricular myocardium; however, right ventricular failure does not necessarily indicate poor right ventricular performance or damage of the right ventricular myocardium, since in the presence of right ventricular failure, maximal right ventricular dp/dt was higher than in control subjects, and right ventricular I/p dp/dt and $V_{MAX}$ did not differ significantly from values measured in control subjects. In the presence of pulmonary hypertension, right ventricular contractile performance is increased, presumably in order to overcome the increased pressure load imposed upon it. When clinical evidence of failure occurs in patients with pulmonary hypertension, the right ventricle may still function in a normal or hypercontractile state, even though the elevated right ventricular end-diastolic pressure exceeds the plasma oncotic level, thereby producing clinical manifestations of right ventricular failure.

A “level of hyperfunction” has been suggested by experiments in pulmonary arterial banded dogs, and an augmented right ventricular dp/dt has been reported in pulmonary hypertension. There are only sparse reports related to observations of right ventricular negative dp/dt. In dogs, following constriction of the pulmonary artery, illustrations suggest that right ventricular negative dp/dt increased except in the final stages of failure accompanied by shock. In a study of patients with cor pulmonale, a
higher negative dp/dt was illustrated in one patient, but no further information about negative dp/dt was given.28

The correlation observed in this study between right ventricular maximal dp/dt and maximal negative dp/dt suggests a dependence of negative dp/dt upon factors which affect isovolumic dp/dt. The augmented contractile response required to maintain flow in the presence of an increased pressure load may also be expected to result in an increased rate of right ventricular isovolumic relaxation, because the characteristics of relaxation constitute an important aspect of the overall functional capabilities of the ventricle. Many of the patients with pulmonary hypertension and all of the patients with pulmonary hypertension and right ventricular failure were treated with digitalis, which presumably would have improved right ventricular contractile performance in these patients; however, the clinical manifestations of right ventricular failure were present in spite of the drug.

There has been speculation that the heart with an excessive pressure load may fail in a clinical sense, yet be composed of adequately performing muscle.29 In view of the observations in this study, it seems that patients with pulmonary hypertensive heart disease may develop right ventricular failure even though the cardiac muscle may continue to perform normally.

There is clinical evidence to support the observations of this study. An accentuated pulmonary component of the second sound is generally thought to occur in pulmonary hypertension, even in the presence of right ventricular failure. We previously demonstrated that the accentuated pulmonary component of the second sound in patients with pulmonary hypertension reflects an augmented rate of development of the diastolic pressure gradient between the pulmonary artery and right ventricle.30 The rate of development of this pressure gradient is primarily dependent on negative dp/dt.31 Therefore, an accentuated second sound, which is generally recognized to be present, implies an augmented right ventricular negative dp/dt.

In conclusion, in pulmonary hypertension the maximal rate of fall of pressure during isovolumic relaxation, as well as the maximal rate of rise of pressure during isovolumic contraction, occurred at higher rates than in normotensive patients, even in the presence of right ventricular failure. Hyperfunction of the right ventricle of such patients presumably is required to overcome the effects of the chronic pressure overload, and the hyperfunction persists, even after the clinical development of right ventricular failure.

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