Power–Afterload Relation in the Failing Human Ventricle

Y. Christopher Chiu, Patricia W. Arand, and John D. Carroll

Animal studies have shown that the power output of the left ventricle is related to afterload by a bell-shaped curve. Furthermore, the normal ventricle operates at the maximum power point, whereas the diseased ventricle operates off the maximum power point because of increased afterload. We studied this relation in eight patients with dilated cardiomyopathy. A high-fidelity catheter with micromanometer pressure and electromagnetic velocity transducers was used to measure blood pressure and flow velocity in the ascending aorta. The latter was converted into volumetric flow by calibrating with the simultaneously determined thermodilution cardiac output. Ventricular power was calculated by dividing the integral of the aortic blood pressure–flow product by the duration of the cardiac cycle. Intravenous nitroprusside was used to alter afterload and the power–afterload relation was obtained by plotting power against mean aortic blood pressure. In all patients, as blood pressure was lowered initially, the power output of the left ventricle increased. As the dose of nitroprusside was increased further, the total power either plateaued or actually decreased. The averaged power and the mean blood pressure at control were 1.00±0.62 W and 92±9.3 mm Hg, respectively. The averaged maximum increase in power with nitroprusside was 22%, to 1.22±0.73 W, and this occurred at a mean pressure of 80±8.8 mm Hg. This study showed that the power–afterload relation in the human ventricle has a maximum power point at some intermediate level of afterload, similar to that found in animal studies. Instead of operating at the maximum power point, the failing ventricle operates far to the right of the peak because of inappropriately elevated afterload. This mismatch between the left ventricle and the arterial circulation resulted in a submaximal transfer of power. Afterload reduction improves power output by an improvement in matching between the left ventricle and the periphery. (Circulation Research 1992;70:530–535)

KEY WORDS • power • afterload • left ventricle

It is well known in muscle physiology that muscular contraction is governed by the force–velocity relation, in which the force generated by the muscle is inversely related to the velocity of fiber shortening by a hyperbola (Figure 1, top panel). When the rate at which the muscle does external work, is given by the product of velocity and force. At the extremes of the force–velocity curve, either force or velocity is zero, and so their product is also zero. Thus, when power is plotted against force (i.e., afterload), the resultant curve is a parabola that approaches zero at extremes of force and rises to a maximum at some intermediate level of force (Figure 1, bottom panel). In the intact ventricle, power output is determined by the product of blood pressure and flow, and no knowledge regarding ventricular geometry or fiber orientation is required. Thus, this concept can be directly extended from the isolated muscle to the intact ventricle. It has been shown in animals that the power–afterload relation indeed is a parabola and that the normal ventricle operates close to the maximum power point for maximum efficiency. Furthermore, when ventricular function was depressed by the injection of microspheres into the coronary circulation, the operating point of the ventricle fell from the maximum power point. Although the power–afterload relation is well known in isolated papillary muscles and intact animal ventricles, it has not been applied to the study of the human ventricle. The current study was designed to apply this concept to human subjects. More specifically, we studied patients with dilated cardiomyopathy to investigate if their power–afterload relation had a shape similar to those in the animals. Furthermore, we wanted to demonstrate the mismatch that exists in congestive heart failure between the left ventricle and the arterial circulation, resulting in the ventricle operating at a point of suboptimal power generation.

Subjects and Methods

The subjects of this study were patients with dilated cardiomyopathy undergoing cardiac catheterization for evaluation of congestive heart failure. Twenty patients were screened, and among them, eight had aortic flow signals that were satisfactory for analysis. There were six men and two women, and they ranged in age from 25 to 52 years. The cardiomyopathy was idiopathic in three patients. In the other patients, there was a history of alcohol...
abuse in four and hypertension in one. Cardiac catheterization revealed that all patients had normal coronary arteries and severe left ventricular dysfunction.

All subjects gave written informed consent to protocols approved by the Clinical Investigation Committee of the University of Chicago.

Cardiac Catheterization

Patients were premedicated with diazepam (5 mg orally). A multisensor micromanometer catheter with one velocity and three pressure transducers (Millar Instruments, Houston, Tex.) was inserted via the femoral artery, and a Swan-Ganz catheter was inserted via the femoral vein. The multisensor catheter was soaked in warm sterile saline for >45 minutes before calibration and insertion. The side port of the arterial sheath was used for pressure reference relative to micromanometer pressure. The transducers on the catheter are located as follows: a pressure transducer at the tip for left ventricular pressure, a pressure and a flow transducer at 5 cm from the tip for ascending aortic pressure and blood velocity, and a pressure transducer at 30 cm from the tip for descending aortic pressure. This last pressure is not used in the present study.

Data Acquisition

The blood pressure and aortic flow signals were recorded along with a limb lead of the electrocardiogram. They were acquired directly by an IBM-PC with an analog-to-digital conversion board (model DT2801, Data Translations) with 12-bit resolution and an input range of 0–10 V. The data were acquired at a rate of 400 Hz, and each recording interval was 12.5 seconds. The data were then stored on floppy diskettes for later analysis.

Protocol

All patients studied were clinically stable. All medications, except for antiarrhythmic drugs, were withheld the morning of the study. Vasodilators were withheld for 24 hours. After placement of the catheters, baseline recordings of left ventricular and aortic pressures, aortic blood flow velocity, electrocardiogram, and thermodilution cardiac output were made. The patients were then given an infusion of nitroprusside at 0.25 µg/kg/min. After 3 minutes of infusion and when the hemodynamic parameters had stabilized, a new set of pressure, flow, and cardiac output data was acquired. The dose of nitroprusside was then increased at increments of 0.25 µg/kg/min, and new recordings were made 3 minutes after each change in dose. Nitroprusside was discontinued when the systolic blood pressure decreased to <90 mm Hg or if the total drop was >25 mm Hg.

Data Analysis

All data analysis was performed using an IBM-PC. The pressure and velocity signals from one data collection (12.5 seconds) were signal-averaged to produce representative waveforms. The velocity signal was converted into volumetric flow by calibrating with the simultaneously obtained thermodilution cardiac output. Instantaneous left ventricular power was obtained by the product of aortic pressure and flow, and total power for the entire cardiac cycle was then determined by integrating the area under the instantaneous power curve and dividing it by the length of the cardiac cycle. Total power was plotted against mean aortic pressure (which is used as an indicator of afterload) to give the power–afterload relation of the left ventricle.

The changes in blood pressure, cardiac index, heart rate, left ventricle end-diastolic pressure, and total power with nitroprusside compared with control were analyzed with the paired t test. A value of p<0.05 was considered statistically significant.

Results

A typical example of the data collected from a patient during nitroprusside infusion is shown in Figure 2. The data included electrocardiogram, aortic blood velocity, and left ventricular ascending and descending aortic pressure waveforms. Only ≈2 seconds of data was shown; the entire data recording interval was 12.5 seconds. The pressure waveforms were excellent in all patients screened, but the velocity signal was not always satisfactory. Only recordings with flat baseline and no significant negative dip during diastole were considered acceptable for analysis. Out of 20 patients studied, eight had excellent velocity signals and were used for the present study. An example of the signal-averaged blood velocity and left ventricular and ascending aortic pressure data is shown in Figure 3. The descending aortic pressure shown in Figure 2 is not used for the current study.

The hemodynamic changes in the patients with the administration of nitroprusside are illustrated in Table
FIGURE 2. Typical example of data acquired from a patient before and during nitroprusside infusion. The tracings in each panel are, from top to bottom, electrocardiogram (ECG), aortic blood flow velocity, and ascending, descending, and left ventricular (LV) pressure. Left panel: The control state. Middle and right panels: During nitroprusside infusion at 0.5 and 0.75 μg/kg/min, respectively.

The average maximum dose of nitroprusside used was 1.22±0.60 μg/kg/min, which produced an average decrease of mean aortic pressure from 92±9.3 to 77±8.7 mm Hg (p<0.05). The average cardiac index increased from 2.39±1.20 to 3.04±1.30 l/min/m² (p<0.05). The heart rate was essentially unchanged, from 94 to 93 beats per minute (p=0.61). The left ventricular end-diastolic pressures decreased slightly with nitroprusside, from 24±6.6 to 20±7.5 mm Hg (p=0.07).

The average maximum increase of total power with nitroprusside infusion was 22% (from 1.00±0.62 to 1.22±0.73 W (p<0.05), Table 2); in all patients, this was achieved before the maximum dose of nitroprusside was reached. As the dose of nitroprusside was increased further, the total power decreased. In two of the patients (Nos. 6 and 8), the total power decreased by >10% from the maximum.

This finding was graphically illustrated in Figure 4, in which the total power of the left ventricle is plotted against mean aortic blood pressure. In all plots, the normal operating points for these patients are on the right end of the graph, with an averaged mean blood pressure of 92±9.3 mm Hg. This is far higher than the optimal afterload (80±8.8 mm Hg) at which the ventricle generated maximum power.

**Discussion**

This is the first study to focus specifically on the power–afterload relation in humans. Although nitroprusside has been shown to improve the power output of the failing ventricle, the fact that further reduction in afterload by increasing the dose of nitroprusside can cause a decrease in the power output has not been well described in the human ventricle. There are ample animal experimental data, both in the isolated papillary muscle and in the intact ventricle, to indicate that the power output of the myocardium is related to afterload by a bell-shaped curve with a power maximum at some intermediate level of afterload. The current study showed that in some patients the total power rose and fell as afterload was reduced; this finding confirms that there is a definite optimal afterload at which the power output is maximum. The reason that a power reduction is not seen at the low afterloads in some patients may be due to the fact that blood pressure was not lowered enough to cause a power decrease.

In animal studies, it has been shown that the normal ventricle operates at the power maximum and that it continues to operate there when heart rate and...
Changes of the ventricle and its variable, ventricular end-diastolic pressure (LVEDP), were used to assess cardiac output, ejection fraction, and other parameters related to myocardial function. Furthermore, in one of the studies, when ventricular function was depressed by injection of microspheres into the coronary circulation, the operating point of the ventricle fell from the apex of the power curve. These observations were independent of preload.

In patients with ventricular failure, the decrease in cardiac output causes a neurohormonally mediated vasoconstriction, resulting in inappropriate elevation of afterload. This will shift the operating point of the ventricle far to the right of the power maximum. The resulting mismatch between the left ventricle and the arterial circulation will cause a submaximal transfer of power. Thus, one benefit of afterload reduction in left ventricular failure is to shift the operating point of the ventricle back toward the power maximum, resulting in increased power output and efficiency of the ventricle. In a study by Yin et al., in which nitroprusside was given to patients with heart failure, they found that, while the left ventricular power increased with nitroprusside infusion, the power output of the right ventricle initially increased but eventually decreased as the dose of nitroprusside was increased. One possible explanation for this is that their patients had predominantly left ventricular failure, resulting in the shift of the left ventricular operating point far to the right of the power maximum, while the right ventricular operating point was only displaced slightly. Thus, when afterload was lowered with nitroprusside, the left ventricular power output increased, but since its operating point was so far to the right of the power maximum, the dose of nitroprusside was not enough to reduce the afterload sufficiently to reach the point where power started to decline. In contrast, the right ventricle operating point was only slightly displaced; the dose of nitroprusside used was enough to show the rise and fall of total power as afterload was being reduced.

The power–afterload relation is unique among the various indexes of ventricular function in that it can define the optimal afterload at which the ventricle should be operating. This will be useful in guiding the use of afterload-reducing agents in the failing ventricle so as to prevent overtreating or undertreating the patient. Furthermore, this relation may be useful in following chronic heart diseases such as aortic or mitral regurgitation. The well-compensated ventricle may continue to operate at the optimal point until it starts to

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Max NP dose (μg/kg/min)</th>
<th>Mean AOP (mm Hg)</th>
<th>CI (l/min/m²)</th>
<th>HR (bpm)</th>
<th>LVEDP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>C</td>
<td>NP</td>
<td>C</td>
<td>NP</td>
</tr>
<tr>
<td>1</td>
<td>0.50</td>
<td>89</td>
<td>71</td>
<td>1.29</td>
<td>2.06</td>
</tr>
<tr>
<td>2</td>
<td>2.00</td>
<td>84</td>
<td>72</td>
<td>1.60</td>
<td>2.05</td>
</tr>
<tr>
<td>3</td>
<td>0.75</td>
<td>89</td>
<td>77</td>
<td>2.08</td>
<td>2.74</td>
</tr>
<tr>
<td>4</td>
<td>0.75</td>
<td>83</td>
<td>76</td>
<td>3.49</td>
<td>3.93</td>
</tr>
<tr>
<td>5</td>
<td>1.75</td>
<td>94</td>
<td>78</td>
<td>1.65</td>
<td>2.20</td>
</tr>
<tr>
<td>6</td>
<td>2.00</td>
<td>91</td>
<td>78</td>
<td>1.22</td>
<td>1.66</td>
</tr>
<tr>
<td>7</td>
<td>1.00</td>
<td>92</td>
<td>69</td>
<td>3.41</td>
<td>4.81</td>
</tr>
<tr>
<td>8</td>
<td>1.00</td>
<td>113</td>
<td>97</td>
<td>4.38</td>
<td>4.85</td>
</tr>
</tbody>
</table>

Mean±SD 1.22±0.60 92±9.3 77±8.7* 2.39±1.20 3.04±1.30* 94±17 93±14† 24±6.6 20±7.5‡

Max, maximum; NP, nitroprusside; AOP, aortic pressure; CI, cardiac index; HR, heart rate in beats per minute (bpm); LVEDP, left ventricular end-diastolic pressure; C, control values (before NP infusion).

*p<0.05, †p=0.61, and ‡p=0.07 vs. control by paired t test.

Table 2. Blood Pressure and Power at the Maximum Power Point and at the Maximum Dose of Nitroprusside

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Max power (mm Hg)</th>
<th>Total power (W)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C</td>
<td>Max</td>
</tr>
<tr>
<td>1</td>
<td>89</td>
<td>77</td>
</tr>
<tr>
<td>2</td>
<td>84</td>
<td>74</td>
</tr>
<tr>
<td>3</td>
<td>89</td>
<td>77</td>
</tr>
<tr>
<td>4</td>
<td>83</td>
<td>76</td>
</tr>
<tr>
<td>5</td>
<td>94</td>
<td>85</td>
</tr>
<tr>
<td>6</td>
<td>91</td>
<td>80</td>
</tr>
<tr>
<td>7</td>
<td>92</td>
<td>71</td>
</tr>
<tr>
<td>8</td>
<td>113</td>
<td>99</td>
</tr>
</tbody>
</table>

Mean±SD 92±9.3 80±8.8* 77±8.7* 1.00±0.62 1.22±0.73* 1.14±0.60*

AOP, aortic pressure; C, control values (before nitroprusside [NP] infusion); Max power, values at the maximum power point; Max NP, values at the maximum dose of NP.

*p<0.05 vs. control by paired t test.
fail, and then the operating point of the ventricle will start to fall off the peak of the power–afterload curve.

Limitations of the Study

The current study used an electromagnetic velocity probe to measure blood velocity, and it was then calibrated into volumetric flow by comparing it with thermodilution cardiac output. This assumes that the velocity profile in the region studied is flat and that there is little change in aortic cross-sectional area over the cardiac cycle. Several studies have shown that the velocity profile at rest in the ascending aorta is, indeed, virtually flat across its diameter.11 Although small changes in aortic cross-sectional area do exist over the cardiac cycle, the magnitude of these changes is small (1–3%), particularly in the cardiomyopathic ventricles with low stroke volumes, and the error introduced should be negligible. The quality of the velocity signal is dependent on many factors, and sometimes the signal is less than optimal. To increase the signal-to-noise ratio, we used signal-averaging techniques in our data analysis to enhance the quality of the signal. Furthermore, only waveforms that have flat baseline and no significant diastolic dip were accepted for analysis.

Considerable controversy exists as to which is the most appropriate parameter of ventricular afterload. Most parameters, such as ventricular wall stress, require knowledge of chamber size and wall thickness and geometric assumptions regarding the ventricle. Detailed knowledge of all these variables is difficult, if not impossible, in human subjects undergoing routine cardiac catheterization. In this study, we used mean aortic pressure as a first approximation of afterload because it is easily measured and is the major determinant of left ventricular afterload.

Objections may be raised concerning the use of drugs to alter afterload, because they may have other effects on the circulatory system. Unfortunately, they are the only easy and safe means available for use in the human subject. Methoxamine and nitroprusside have been widely used for this purpose and have been shown to have minimal effects on myocardial contractility.12,13

**Figure 4.** Power–afterload relations. The numbers correspond to the patients listed in Tables 1 and 2. In all the plots, the control state is the point on the right end of the graph with the highest blood pressure. As pressure is decreased with nitroprusside, power increases and then plateaus or even decreases in some patients.
Previous studies with nitroprusside have shown no significant changes in heart rate; this was also the case in the current study (Table 1).

In the isolated papillary muscle, the instantaneous force–velocity and force–power curves shift to different levels if the initial muscle length (preload) is changed. But in the ventricle, it was found empirically that, in the physiological range, some ventricular parameters are relatively preload independent. In general, these are more likely to be ejection-phase rather than isovolumic-phase indexes. Even though total power is an ejection-phase parameter, it is unclear how dependent it is on preload. It could be argued that the decline in power output in some of the patients is due to the decrease in preload with the infusion of nitroprusside. This is unlikely because previous studies have shown that nitroprusside does not significantly alter angiographically and echocardiographically determined diastolic volume. Finally, the change in preload is modest at best, and the left ventricle end-diastolic pressures remained elevated in most of our patients even at the peak dose of nitroprusside.

In summary, this study has shown that the power–afterload relation in the human ventricle has a maximum power point at some intermediate level of afterload, similar to that found in animal studies. The failing ventricle operates far to the right of the power maximum because of inappropriately elevated afterload. Further study in normal hearts will be needed to determine if the healthy human ventricle operates at the maximum power point, as is the case in animal studies. If this is confirmed, the unique feature of the power–afterload relation in defining the optimal afterload will be useful in guiding treatment and monitoring of various heart diseases.

References

Power-afterload relation in the failing human ventricle.
Y C Chiu, P W Arand and J D Carroll

Circ Res. 1992;70:530-535
doi: 10.1161/01.RES.70.3.530

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1992 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/70/3/530

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org/subscriptions/