PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE **185**, 339–346 (1987)

The Right Ventricular Working Heart Preparation (42554)

PAUL M. WERCHAN AND KATHLEEN H. McDONOUGH

Department of Physiology, Louisiana State University Medical Center, New Orleans, Louisiana 70112

Abstract. An isolated working rat heart preparation was modified to study right ventricular (RV) performance. All hearts were perfused with a Krebs–Henseleit bicarbonate buffer via a Langendorff column at 90 mm Hg. Right atrial filling (preload) was varied by raising a buffer reservoir from 5 cm below to 10 cm above the right atrium while pulmonary artery outflow resistance remained fixed. RV systolic pressure and the maximum rise and decrease in pressure development (±dP/dt) were measured via a catheter in the RV. Cardiac output was collected with a catheter placed in the pulmonary artery. One group of hearts, monitored at a fixed preload (0 cm H_2O) for 2 hr, and another group of hearts, in which two ventricular function curves were performed, demonstrated the stability and reproducibility of the preparation. Additionally, the ability of this preparation to measure changes in inotropy was studied. A negative inotropic effect was measured after verapamil (5×10^{-8} *M*) treatment. Positive *dP/dt* showed the greatest depression (30%) and was significantly lower at every preload. A positive inotropic effect was demonstrated by reducing the buffer Ca^{2+} concentration to 1.9 m*M* for the first work curve followed by an addition of Ca^{2+} (2.8 m*M* final concentration) or ouabain (5×10^{-5} *M*) for the second work curve. Again, the greatest effect was found in the *dP/dt* measurements (elevated by 20 and 30%, respectively). Thus, this preparation manifests qualities similar to those used in studying the left ventricle and allows investigation of various cardiac diseases which may affect RV pump function.

The isolated working heart preparation has been used by numerous investigators to study the performance of hearts exposed to a wide variety of pathological or beneficial conditions. These include: ischemia (1), drug additions (2, 3), shock (4), thermal trauma (5), sepsis (6), hypoxia (7), hypertrophy (8–11), exercise (12), and diabetes (13, 14). Under all of these conditions only left ventricular performance has been measured. Little or no attention has been given to the right ventricle (RV) under most circumstances although it is possible that the two ventricles may respond differently. For example, biochemical and contractile function studies of myocardial hypertrophy have shown that the right ventricle may develop a physiological hypertrophy in response to a pressure overload whereas the left ventricle (LV) may exhibit a pathological hypertrophy (15). In addition, right ventricular dysfunction in patients following resuscitation from hypovolumic and septic shock may be of more clinical concern than the dysfunction of the left ventricle (16). For this reason the isolated working heart preparation was modified to study right ventricular performance. This preparation is stable for at least 2 hr, demonstrates Frank–Starling characteristics, and can measure significant changes in contractility with positive and negative inotropic drugs or with changes in the calcium concentration of the buffer.

Materials and Methods. A working heart apparatus (Fig. 1) was used to study right ventricular function. All glass columns used in the apparatus were jacketed and the circulating water temperature was maintained at 37°C. The Langendorff column (A) was filled with a Krebs–Henseleit bicarbonate (KHB) buffer, which consisted of the following (m*M*): NaCl, 118; KCl, 4.7; $MgSO_4$, 2.4; KH_2PO_4, 1.2; $NaHCO_3$, 25; Na EDTA, 0.5; $CaCl_2$, 2.8; and glucose, 10. Buffer was gassed with 95% O_2:5% CO_2 and maintained at 37°C. The height of the buffer in the Langendorff column could be controlled by raising or lowering the outflow tube extending into the buffer. For all experiments, the height of this column was set to deliver 90 mm Hg of perfusion pressure at the aortic cannula opening. For determination of coronary flow, buffer was pumped into the Langendorff column at a known, constant rate. When a coronary flow measurement was desired, the overflow from the Lagendorff column was collected in a graduated cylinder for 1 min. Coronary flow was calculated using the formula

0037-9727/87 $1.50

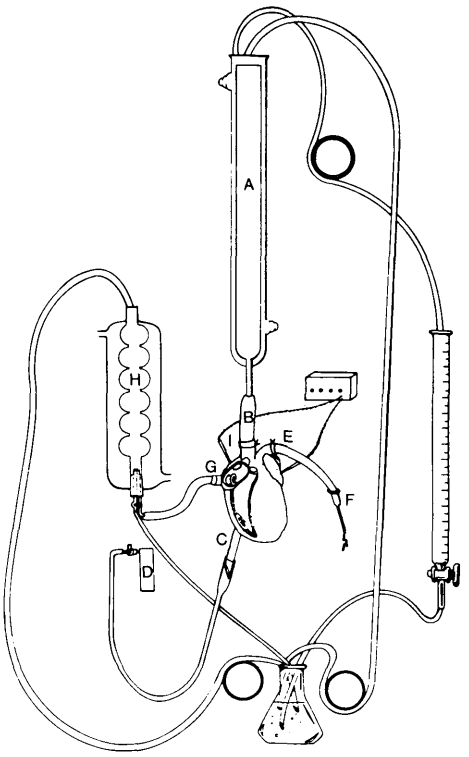

FIG. 1. Diagram of the isolated working heart apparatus modified to study the right ventricle. A = Langendorff column for retrograde perfusion of the coronary arteries; B = aortic cannula; C = right ventricular cannula; D = Stathan ID23 pressure transducer attached to a Grass Model 7 polygraph; E = pulmonary artery cannula; F = pulmonary artery outflow resistance as set by an 18-gauge needle; G = right atrial catheter; H = right atrial filling reservoir; and I = pacing electrodes.

Coronary flow (ml/min)

= Langendorff inflow (ml/min)

− Langendorff overflow (ml/min).

Male Sprague–Dawley rats (300 g) were anesthetized with pentobarbital (60 mg/kg), the thorax was opened, the aorta was cut at the beginning of the aortic curvature, and the heart was removed and placed into cold (4°C) saline. The aorta was tied securely to the aortic cannula (B) leading to the Langendorff column. Maximal flow was then initiated through the cannula. The first of three catheters to be placed in the heart was a short piece (4 cm) of PE60 tubing (C) with a point at one end and a flare at the other. The pointed end was directed into the inferior vena cava. Once in the right atrium, the heart was tilted slightly so that the catheter could slide through the tricuspid valve and enter the right ventricle. When the apex of the right ventricle was reached, the pointed end of the catheter was pushed through the free wall. The entire catheter was pulled through until the flared end reached the endocardium and resistance was felt. The pointed end was inserted into the end of a larger diameter tube leading to the pressure transducer (D) (Statham ID23) attached to a Grass Model 7 polygraph. A ligature was placed under the pulmonary artery and pushed through the connective tissue located between the pulmonary artery and the aorta. While the left pulmonary artery was occluded, the right pulmonary artery was cut just at the branch point, allowing for a stainless-steel curved cannula (E) to be placed into the main pulmonary artery and tied securely. An additional ligature was tied distal to the first. The catheter was extended from the heart and an 18-gauge needle (F) was placed at the end to partially set outflow resistance. Needle placement above the heart additionally affects resistance and thus ventricular performance. For this study, the needle was placed at heart level for all groups. The buffer collected for 1 min via this catheter was the cardiac output.

Next, the openings of the superior vena cava and the thoracic veins were located, occluded, and ligated. Effluent from the coronary sinus filled the right atrium and caused the inferior vena cava to open. This allowed easier access for the last catheter (G) to be placed and tied. This catheter was attached to the right atrial filling chamber (H) which could be raised or lowered and thus fill or withdraw from the right atrium.

Finally, pacing electrodes (I) were placed on the left atrial appendage and the superior vena cava and hearts were paced at 300 beats per minute (bpm) with a Grass SD9 stimulator. A water jacket was placed around the heart to help maintain temperature at 37°C. Total time for this procedure was approximately 30 min.

Specific protocols for RV performance. Five groups of experiments were designed to demonstrate that both positive and negative changes in inotropy could be measured using

the right ventricular working heart apparatus. Right ventricular systolic pressure (RVSP), cardiac output (CO), and positive and negative dP/dt_{max} were measured at each preload and served as indices of right ventricular performance. Group 1 (n = 6) consisted of hearts monitored for 2 hr at one preload (0 cm H_2O right atrial filling pressure, RAFP). In group 2 (n = 9), two identical work curves were performed on each heart (eight preloads ranging from −5 to +10 cm H_2O RAFP). For groups 3–5, two work curves were also performed on each heart (five or eight preloads). However, in these three groups, one ventricular function curve was generated followed by a second work curve in which a change was made in the buffer composition. The second work curve for group 3 (n = 8) was performed after the addition of verapamil (5×10^{-8} M) to the KHB buffer (2.8 mM Ca^{2+}). In groups 4 (n = 8) and 5 (n = 5) the initial work curve used KHB buffer with a lower (1.9 mM) Ca^{2+} concentration. Additions of Ca^{2+} (2.8 mM final) and ouabain (5×10^{-5} M) were made just before the second work curve in groups 4 and 5, respectively.

Statistics. A one-way ANOVA with repeated measures was performed for group 1. For groups 2–5, a paired t test was performed on the first and second work curves at each preload. Values were considered significantly different when $p < 0.05$.

Results. As in previous Langendorff buffer perfused heart preparations, high coronary flows are necessary for adequate metabolic support. A majority of this volume returns as venous effluent to the coronary sinus located in the right atrium. This volume was sufficient to maximize filling of the right ventricle. In order to lower right ventricular filling, the right atrial filling chamber was placed below the level of the heart in order to siphon buffer from the right atrium.

At a preload of 0 cm H_2O RAFP, no significant changes occurred in RVSP, CO, $+dP/dt$, or $-dP/dt$ at any time point for 2 hr (Fig. 2). In groups 2–5, all four variables were responsive to alterations in preload and hearts exhibited typical Frank–Starling relationships (Table I). The greatest change in these variables occurred in a narrow preload range from −2.5 to +2.5 cm H_2O. Most hearts tended to reach a plateau above and below these points. At each preload change the hearts rapidly stabilized. The RVSP generated by these hearts spanned a physiological range for the RV *in vivo*. In contrast, the cardiac outputs were only about 10% of those measured in rats with the same size hearts (17).

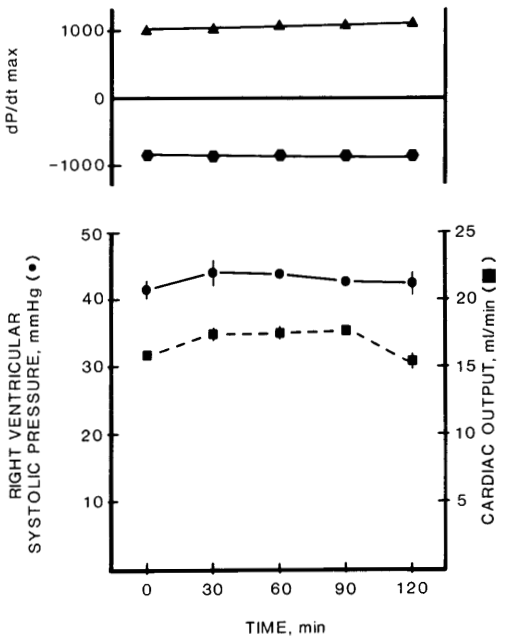

FIG. 2. *In vitro* right ventricular performance monitored for 2 hr at a fixed preload (0 cm H_2O): RVSP = right ventricular systolic pressure. dP/dt is the maximum rate of pressure development (+) and pressure decline (−). Values are expressed as means ± SEM (n = 6). No values were significantly different.

As a further indication of reproducibility and stability of the hearts using this preparation, a second curve, using the same preloads as those in the first, was performed. RVSP and CO changed by an average of 5.8 and 15%, respectively. Statistically, only three of nine preloads for either RVSP or CO were different. Greater stability was obtained with the $\pm dP/dt_{max}$ measurements (Fig. 3) in which the second curves were different by only 3–4%. Also, no values from the first and second curves were different at any preload.

Group 3: verapamil. A slow Ca^{2+} channel blocker was used to determine whether this preparation could measure negative inotropic responses. A depression was recorded for all four variables and ranged from 22 to 30%. The greatest depression was seen in positive $dP/$

TABLE I. COMPARISON OF FIRST AND SECOND WORK CURVES FOLLOWING NO CHANGE IN BUFFER COMPOSITION OR ADDITION OF VERAPAMIL

		Work curve	Right atrial filling pressure (cm H_2O)						
			−5.0	−2.5	−1.25	0	2.5	5.0	7.5	10.0
Group 2 (no addition)	RVSP	First	24.6 ± 2.1	27.2 ± 2.5	33.5 ± 2.4	40.3 ± 3.4	47.2 ± 3.3	49.3 ± 2.8	49.9 ± 2.1	49.5 ± 2.2
		Second	25.1 ± 2.3	25.3 ± 2.6*	32.4 ± 2.2	36.9 ± 3.0*	40.1 ± 3.9	45.7 ± 2.6	46.7 ± 2.2*	47.5 ± 1.9
	CO	First	4.0 ± 0.6	5.5 ± 0.7	8.4 ± 0.7	11.9 ± 1.4	15.7 ± 1.4	17.2 ± 1.2	18.2 ± 1.1	18.3 ± 1.0
		Second	3.5 ± 0.5	4.2 ± 0.8*	7.2 ± 0.7	10.7 ± 1.1*	13.9 ± 1.3	15.6 ± 1.2	16.8 ± 1.1	17.6 ± 1.0*
Group 3 (verapamil)	RVSP	No verapamil	20.3 ± 1.1	25.5 ± 1.7	38.6 ± 0.8	43.6 ± 3.1	51.0 ± 2.4	54.1 ± 2.3	56.9 ± 2.1	59.6 ± 2.8
		Plus verapamil	18.1 ± 1.1	18.4 ± 1.5*	23.9 ± 2.6*	29.1 ± 2.0*	36.9 ± 2.9*	40.4 ± 2.7*	42.2 ± 2.8*	43.3 ± 2.6*
	CO	No verapamil	3.5 ± 0.6	5.6 ± 0.5	9.5 ± 1.2	11.8 ± 0.8	15.5 ± 0.9	17.6 ± 0.9	19.2 ± 0.8	20.6 ± 1.1
		Plus verapamil	3.3 ± 0.5	4.2 ± 0.8	5.8 ± 1.0	9.2 ± 0.7*	12.6 ± 1.2*	14.4 ± 1.2*	15.2 ± 1.3*	16.0 ± 1.2*

Note. Values are expressed as means ± SEM. RVSP = right ventricular systolic pressure; CO = cardiac output. *$P < 0.05$; the value from the second curve is different from the value of the first curve or the verapamil value is different from no verapamil value.

dt_{max}, which was significantly lower at every preload (Fig. 4).

Group 4: low and high calcium. The initial work curve of this group was depressed due to the lowered free Ca^{2+} concentration of the buffer. However, this depression averaged only 12% ($+dP/dt$) in comparison to the first work curves of group 2. Also, there was a trend for the lowest preloads (−5 and −2.5 cm H_2O) to be more affected (35 and 17% depression, respectively) by the lowered Ca^{2+}. When additional Ca^{2+} was supplied (2.8 m*M*), function improved and the greatest increase occurred at −5 and −2.5 cm H_2O (41.4 and 41.7% increases in $+dP/dt$ compared to the first curve) (Fig. 5). Overall, a 22–26% increase was measured for all four variables and the increase was significantly different at most preloads (Table II).

Group 5: ouabain with 1.9 mM Ca^{2+}. The positive inotropic effects for this group matched those seen in the Ca^{2+} study (group 4). Right ventricular systolic pressure, $+dP/dt$, and $-dP/dt$ (Fig. 6) were increased by ouabain. The greatest effects were seen at the two lowest preloads (30–49.8% increase from the first curve). The average effect for the whole work curve ranged from 23 to 30%. However, these increases were only significant at two ($-dP/dt$) or three ($+dP/dt$) of the five preloads. In contrast, no significant changes were measured in cardiac output at any preload (Table II).

Coronary flow. In a separate group of hearts ($n = 5$) coronary flow was determined throughout the entire work curve followed by a repeat of the −5 cm H_2O preload. Although coronary flow tended to increase with an increase in preload (work), the change was not significant (Fig. 7).

Discussion. In this study, the isolated working heart preparation was modified to study the performance of the rat right ventricle. In the past, the preparation has been used exclusively to study LV performance. The RV preparation has a modification distinguishing it from the LV preparation. Hearts receive retrograde coronary flow from a Langendorff column at a perfusion pressure of 90 mm Hg throughout the entire protocol. In contrast, in LV working heart studies, as under *in vivo* conditions, the heart relies upon LV performance to maintain coronary perfusion pres-

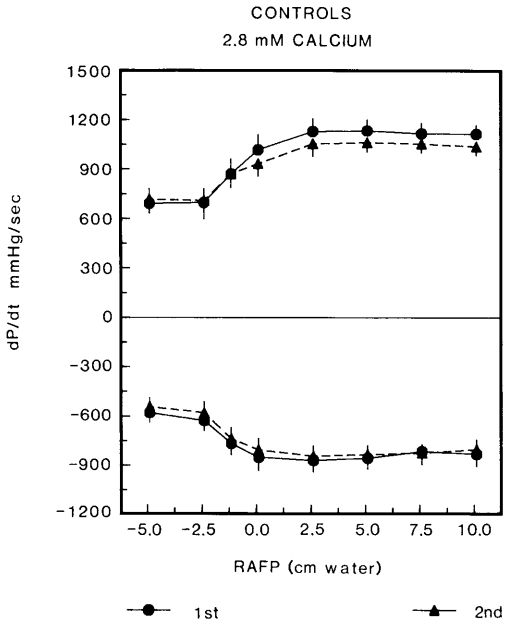

FIG. 3. *In vitro* right ventricular performance as a function of right atrial filling pressure: $\pm dP/dt$ is the maximum rate of pressure development and pressure decline. Values expressed as means ± SEM (n = 9). No values were significantly different.

sure and thus coronary flow. Depression of cardiac performance (such as in sepsis or diabetes) may occur in conjunction with decreased coronary flow which could lead to further depression of cardiac performance. When this occurs it is difficult to interpret whether the dysfunction is due to inadequate perfusion, to altered muscle mechanics, or to a combination of the two. In the right ventricular preparation, coronary flow is relatively constant such that changes in ventricular function can be attributed to direct cardiac effects. We have, however, measured decreases in coronary flow in the RV preparation. These changes were partially reversed by the addition of adenosine to the perfusion buffer (data not shown). This would indicate that these hearts may have the ability to autoregulate. Since coronary flow can change in parallel to the workload demand of the heart, flow probably never limits cardiac performance. It should be emphasized that these are measurements of total coronary flow (both RV and LV) and, therefore, this preparation cannot directly determine RV coronary flow or O_2 consumption.

The stability of this preparation was demonstrated in two ways. In group 1, ventricular performance was stable for 2 hr. In group 2, two consecutive work curves were performed on the same heart. At most preloads no significant changes were found in RVSP, CO, and especially *dP/dt*. As a result, the *dP/dt* measurement was used in the analysis of changes in inotropy in this study.

In these experiments the RV exhibited the typical Frank–Starling relationship found in the LV (18). However, RV ventricular function curves are shifted far to the left and are very sensitive to any change in preload between −2.5 and 2.5 cm H_2O RAFP. The sensitivity is identical to that measured for the dog RV *in vivo* (19). However, these hearts are never capable of the same cardiac outputs measured for rats *in vivo*. One probable cause for this is the lack of a normally functioning LV and the normal interplay between the two ventricles that is thought to occur *in vivo*. It is known that a Langendorff perfused LV can develop at least enough pressure to match perfusion pressure and thus open the aortic valve

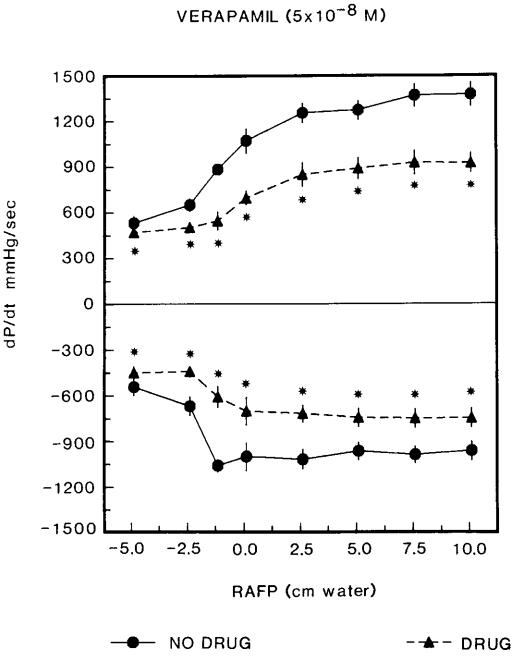

FIG. 4. *In vitro* right ventricular performance ($\pm dP/dt_{max}$) as a function of right atrial filling pressure before and after the addition of verapamil (5×10^{-8} *M*). Values expressed as means ± SEM (n = 8). *Indicates values significantly different at each preload before and after drug addition.

TABLE II. COMPARISON OF FIRST AND SECOND WORK CURVES FOLLOWING CHANGES IN BUFFER COMPOSITION

			Right atrial filling pressure (cm H_2O)				
		Work curve	−5.0	−2.5	0.0	5.0	10.0
Group 4 (calcium)	RVSP	Low calcium	17.4 ± 1.5	24.4 ± 2.1	39.9 ± 3.8	49.1 ± 3.5	50.4 ± 9.0
		High calcium	24.2 ± 1.9*	32.7 ± 3.8	45.6 ± 3.7*	54.3 ± 2.6*	56.9 ± 3.3*
	CO	Low calcium	2.8 ± 0.5	5.3 ± 0.8	11.0 ± 0.4	13.9 ± 0.8	15.1 ± 1.8
		High calcium	4.1 ± 0.5*	7.1 ± 0.6	12.0 ± 0.6*	16.2 ± 0.6*	17.6 ± 0.7
Group 5 (ouabain)	RVSP	No ouabain	21.4 ± 1.8	24.0 ± 3.1	39.1 ± 3.9	46.7 ± 4.6	48.0 ± 5.3
		Plus ouabain	30.3 ± 2.7	31.2 ± 1.1	44.7 ± 4.0*	52.8 ± 3.9*	54.5 ± 4.6
	CO	No ouabain	3.9 ± 1.2	5.6 ± 1.0	12.4 ± 1.3	16.8 ± 1.7	18.5 ± 2.2
		Plus ouabain	4.4 ± 0.7	5.5 ± 0.4	12.2 ± 1.4	17.9 ± 1.9	19.5 ± 2.2

Note. Values are expressed as means ± SEM. *$P < 0.05$; values of the high calcium curve that are significantly different from the low calcium curve or the ouabain value is different from no ouabain value. RVSP = right ventricular systolic pressure; CO = cardiac output.

(20). This would suggest that the LV may contribute to RV function in this preparation. However, this contribution is probably minimal since the LV is not pumping fluid. Low cardiac output could also be explained if there were a greater resistance to cardiac output in this *in vitro* preparation than in the whole animal. If so, a greater percentage of contractile energy would be used during the period of isovolumic contraction and less would be avail-

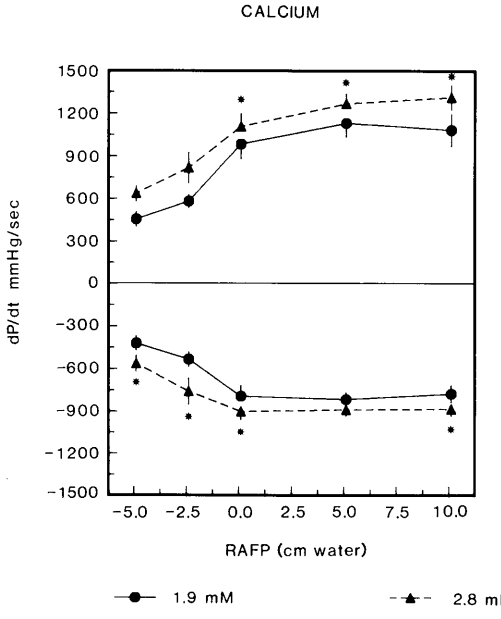

FIG. 5. *In vitro* right ventricular performance ($\pm dP/dt_{max}$) as a function of right atrial filling pressure with low (1.9 m*M*) and high (2.8 m*M*) calcium concentrations. Values expressed as means ± SEM ($n = 8$). *Indicates values significantly different at each preload for the two calcium concentrations.

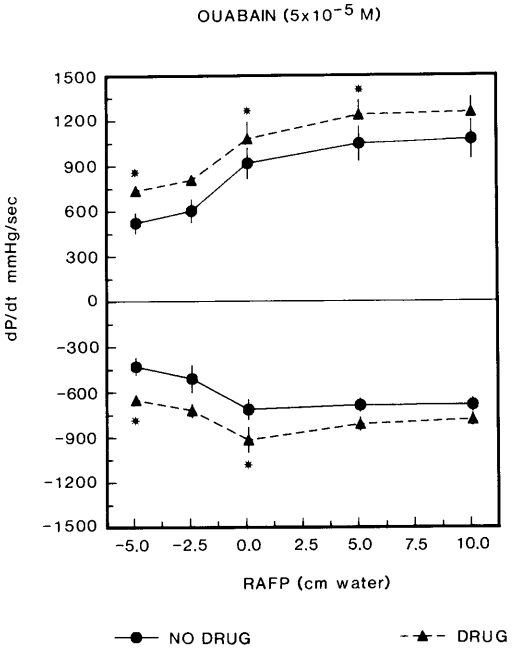

FIG. 6. *In vitro* right ventricular performance ($\pm dP/dt_{max}$) as a function of right atrial filling pressure before and after the addition of ouabain (5×10^{-5} *M*) with a low (1.9 m*M*) calcium concentration. Values expressed as means ± SEM ($n = 5$). *Indicates values significantly different at each preload before and after drug addition.

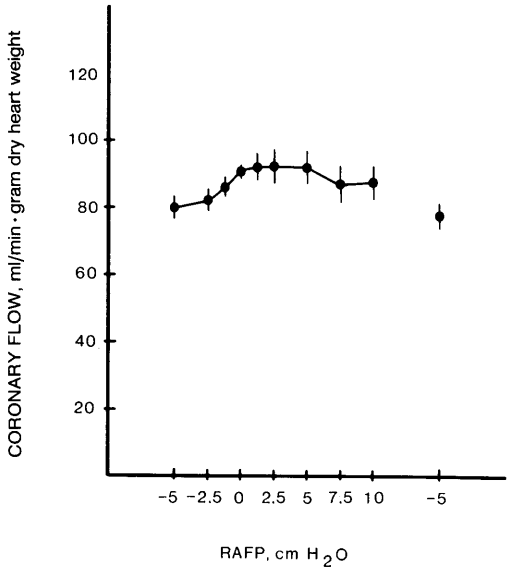

FIG. 7. *In vitro* coronary flow normalized to total dry weight of the heart as a function of right atrial filling pressure (n = 5). Values expressed as means ± SEM. No values were significantly different from each other.

able for myocardial fiber shortening and thus cardiac output. Any reduction in the outflow resistance should, and does, lead to an increase in the cardiac output. Even though a systematic study of afterload was not made, a reduction in outflow resistance by increasing needle size decreased pressure development and increased cardiac output. Lowering resistance by dropping the outflow needle below the level of the heart was not desirable since a "siphon effect" could possibly occur, thus elevating and overestimating cardiac output.

Changes in the inotropic state of the right ventricle with verapamil and calcium additions occurred as expected. Thus we were assured that we could measure negative and positive inotropic responses, respectively, using our modified working heart preparation. In a further attempt to show a positive inotropic effect, ouabain was added to a group of hearts at a dose which produced a small (13.6%) but significant elevation in CO × PSP (at the lowest preload) of control isolated working left ventricles (18). This dose of ouabain (1×10^{-5} M) had no effect upon the RV (data not shown). However, calcium availability may have already been maximized at the 2.8 mM calcium concentration used in this study. Therefore, in another series of hearts, calcium was reduced to 1.9 mM for the first work curve and ouabain was added for the second (group 5). Although quantitatively different, these experiments were qualitatively similar to those of McDonough *et al.* (18). Both studies showed the greatest elevations in PSP at the lowest preloads with no changes in cardiac output at any preload. The lesser response at high preloads may result from increased stretching of the myocardium at high preloads causing an increased calcium entry into the cell. Thus, if Ca^{2+} entry is already maximum, a ouabain-induced Ca^{2+} entry may not alter contractile performance.

In conclusion, with the working heart preparation we could measure both positive and negative inotropic responses of the RV. This preparation was stable for at least 2 hr and allowed the measurements of RVSP, CO, and $\pm dP/dt$ at various fixed preloads. Positive and negative dP/dt_{max} were the most reliable indicators of a change in contractility.

1. Neely JR, Rovetto MJ, Whitmer JT, Morgan HE. Effects of ischemia on function and metabolism of the isolated working rat heart. Amer J Physiol **225:** 651–658, 1973.
2. Adams HR, Parker JL, Mathew BP. The influence of ketamine on inotropic and chronotropic responsiveness of heart muscle. J Pharmacol Exp Ther **201:**171–183, 1977.
3. Adams HR, Rhody J, Sutko JL. Amrinone activates K^+-depolarized atrial and ventricular myocardium of guinea pigs. Circ Res **51:**662–665, 1982.
4. Parker JL, Adams HR. Myocardial effects of endotoxin shock: Characterization of an isolated heart muscle model. Adv Shock Res **2:**163–175, 1979.
5. Temples TE, Burns AH, Nance FC, Miller HI. Effect of burn shock on myocardial function in guinea pigs. Circ Shock **14:**81–92, 1984.
6. McDonough KH, Lang CH, Spitzer JJ. Depressed function of isolated hearts from hyperdynamic septic rats. Circ Shock **12:**241–251, 1984.
7. Rovetto MJ, Whitmer JT, Neely JR. Comparison of the effects of anoxia and whole heart ischemia on carbohydrate utilization in isolated working rat hearts. Circ Res **32:**699–711, 1973.
8. Hallback M, Isaksson O, Noresson E. Consequences of myocardial structural adaptation on left ventricular compliance and the Frank–Starling relationship in spontaneously hypertensive rats. Acta Physiol Scand **94:**259–270, 1975.
9. Noresson E, Rickstein SE, Hallback-Norlander M, Thoren P. Performance of the hypertrophied left ventricle in spontaneously hypertensive rat. Effects of

changes in preload and afterload. Acta Physiol Scand **107**:1–8, 1979.
10. Heller LJ. Isovolumetric properties of ventricles of spontaneously hypertensive rats. Amer J Physiol **240**: H927–H933, 1981.
11. Burns AH, Montini J. Myocardium in hypertrophy: Oxygen consumption by isolated cardiac myocytes and working hearts from spontaneously hypertensive rats. Life Sci **30**:29–37, 1982.
12. Schaible TF, Scheuer J. Cardiac function in hypertrophied hearts from chronically exercised female rats. J Appl Physiol **50**:1140–1145, 1981.
13. Garber DW, Everett AW, Neely JR. Cardiac function and myosin ATPase in diabetic rats treated with insulin, T_3 and T_4. Amer J Physiol **244**:H592–H598, 1983.
14. Vadlamudi RVSV, McNeill JH. Effect of experimental diabetes on isolated rat heart responsiveness to isoproterenol. Canad J Pharmacol **62**:124–131, 1983.
15. Wikman-Coffelt J, Mason DT. Myosin characteristics and immunological properties of myocardial tissue. In: Riecker G., Weber A., Goodwin G., Eds. Myocardial Failure. New York: Springer-Verlag, pp52–67, 1977.
16. Hoffman MJ, Greenfield LJ, Sugerman HJ, Tatum JL. Unsuspected right ventricular dysfunction in shock and sepsis. Ann Surg **198**:307–319, 1983.
17. McNabb LJ, Baldwin KM. Hemodynamic and metabolic effects of exercise in Crotalaria-induced pulmonary hypertension in rats. J Appl Physiol **57**:1829–1833, 1984.
18. McDonough KH, Lang CH, Spitzer JJ. Effect of cardiotropic agents on the myocardial dysfunction of hyperdynamic sepsis. Circ Shock **17**:1–19, 1985.
19. Guyton AC. Textbook of Medical Physiology. Philadelphia; Saunders, Vol 5, p171, 1976.
20. Neely JR, Liebermeister H, Battersby EJ, Morgan HE. Effect of pressure development on oxygen consumption by isolated rat heart. Amer J Physiol **212**:804–814, 1967.

Received January 12, 1987. P.S.E.B.M. 1987, Vol. 185.
Accepted April 3, 1987.