Unsuspected Right Ventricular Dysfunction in Shock and Sepsis

MICHAEL J. HOFFMAN, M.D., LAZAR J. GREENFIELD, M.D.,
HARVEY J. SUGERMAN, M.D., JAMES L. TATUM, M.D.

From the Departments of Surgery and Radiology, Medical College of Virginia, Virginia Commonwealth University, Richmond, Virginia

Monitoring of ventricular function by central venous (CVP) and pulmonary wedge pressures (PCW) was compared with ejection fraction and end-diastolic volume (gated pool scan) in patients resuscitated from hypovolemic and septic shock. Sixteen patients were studied within 24 hours of resuscitation and all showed depressed right ventricular ejection (RVEF) and/or an increased end-diastolic volume (RVEDVI). Group I (eight patients, hypovolemia and sepsis) had low RVEF (mean, 0.30), high RVEDVI (mean 129.2 ml/m^2), and nearly normal left ventricular function (LVEF 0.63 and LVEDVI 63.6 ml/m^2), compared to angiographic normals (RVEF 0.52, RVEDVI 55.8 ml/m^2; nL LVEF 0.59, LVEDVI 52.3 ml/m^2). Group II (3 patients, all septic) had better RVEF (mean, 0.54) but high RVEDVI (mean, 121.1 ml/m^2) with normal LVEF (mean, 0.67) and high LVEDVI (mean LVEDVI 107.2 ml/m^2). Group III consisted of five patients (hypovolemia and sepsis) who had biventricular depression (RVEF 0.25 and LVEF 0.29) and elevated EDVI. The mortality rate for group I (25%) was significantly less than for groups II and III (100% and 80%, respectively), and could be correlated with failure to improve RV function. Follow-up studies in ten patients showed improvement in seven which correlated with increased RVEF and reduced RVEDVI. Comparing survivors to non-survivors showed no predictability on the basis of initial studies but a significantly larger RVEDVI and RV stroke work index in non-survivors' follow-up studies. No correlation could be made with left ventricular performance, and there were no correlations between PCWP and LVEDVI or CVP and RVEDVI. A significant negative correlation was seen between RVEF and pulmonary vascular resistance ($r = -0.34$, $p < 0.05$). Both LVEDVI and RVEDVI were correlated significantly with cardiac index and with each other. RV dysfunction occurs after resuscitation of hypovolemia and sepsis without reliable alteration in filling pressure and is likely related to myocardial ischemia as well as increased pulmonary vascular resistance. Survival seems to depend on improvement in RV performance, which can be measured at the bedside by cardiac scintigraphy.

THERE IS increasing evidence that the traditional methods of monitoring fluid resuscitation using central venous pressure (CVP) and pulmonary capillary wedge pressure (PCWP) may be inadequate for regulating resuscitation and preventing ventricular overload.[1-4] Specifically, Baek et al.[2] showed no correlation between PCWP and left ventricular end-diastolic volume (LVEDV) in patients undergoing myocardial revascularization. The importance of end-diastolic volume relates to the Frank-Starling principle that increased stretch of the myocardium by increased ventricular volume will produce increased contractile force and stroke volume within certain limitations.[5] However, the relationship between filling pressure and end-diastolic volume depends on the compliance of the ventricle, and a change in filling pressure may reflect a change in ventricular volume or compliance or both.

Calvin et al.[4] pointed out that critically ill patients requiring volume resuscitation will have different ventricular compliance curves, and similar changes in pressure-volume relationships have been shown by others to occur acutely under a variety of different conditions.[3,6,7]

Martyn et al.[8] showed that in a group of burned patients, the right ventricular end-diastolic volume (RVEDV) was a better predictor of cardiac index than urine output, PCWP, or CVP. Right ventricular dysfunction was also found in burned patients after resuscitation and was felt to jeopardize survival.[9] Right ventricular distention within a normal pericardium can alter left ventricular compliance and function by shift of the septum[10] or by inducing myocardial ischemia.[11]

With this demonstration of RV dysfunction after thermal injury, it seemed likely that this problem could occur in patients with other forms of shock. Therefore, we studied 16 patients after resuscitation from hypovolemic or septic shock using equilibrium-gated cardiac scintigraphy and thermodilution techniques to determine the right and left ventricular ejection fractions and end-di-

Presented at the Annual Meeting of the American Surgical Association, May 12-14, 1983, Boca Raton, Florida.

Reprint requests: Lazar J. Greenfield, M.D., P.O. Box 645, MCV Station, Richmond, Virginia 23298.

Submitted for publication: May 16, 1983.

0003-4932/83/0900/0307 $01.45

astolic volumes as well as more conventional measurements used to monitor critically ill patients.

Materials and Methods

Patient Classification

Nine patients (four male, five female), ranging in age from 36 to 72 years, who had septic shock and seven patients (six male, one female) ranging in age from 16 to 78 years who had hypovolemic shock were studied within 24 hours of resuscitation. Shock was defined as a systolic blood pressure less than 80 mmHg. In addition, seven patients who had undergone elective operations requiring at least 6 L of fluid replacement but with no hypotension were studied within 24 hours after operation. There were three men and four women in this control group, ranging in age from 60 to 81 years. In all cases, arterial P_{O_2} was maintained greater than 65 mmHg with P_{CO_2} less than 45 mmHg. Eighteen of the total of 23 patients required mechanical ventilation. The incidence of known cardiac disease was similar in each group and was found in two of seven control patients (29%), one of seven hypovolemic patients (14%), and two of nine septic patients (22%). Their history of cardiac disease included past myocardial infarction, angina, or cardiomyopathy. Control patients generally underwent major vascular procedures, whereas the septic and hypovolemic patients had a variety of clinical diagnoses (Tables 1–3). All patients had a triple lumen pulmonary arterial catheter in place (Gould CritiCath Model SP-107).

Resuscitation was monitored initially by standard measurements of blood pressure, heart rate, urine output, CVP and PCWP. Nine patients were restudied 2 to 4 days after the initial study (5 hypovolemic, 4 septic) and two patients had a second follow-up study. The patients who had follow-up studies were grouped initially according to ventricular function and then according to whether they had shown clinical deterioration (N = 3) or improvement (N = 7), based on blood pressure, urine output, cardiac output, mental status, need for vasopressors or mechanical ventilation, and survival.

Measurements and Calculations

Each study consisted of the simultaneous measurement of left ventricular ejection fraction (LVEF) and right ventricular ejection fraction (RVEF) by gated cardiac scintigraphy as well as measurement of blood pressure, heart rate, pulmonary artery pressure (PA), CVP, PCWP, and cardiac output. Pressure measurements were made using a Statham P-23 ID transducer and an oscilloscopic recorder (Electronics for Medicine).

TABLE 1. *Operative Procedures in Control Patients*

	Patients
Abdominal aortic aneurysm repair	3
Thoracic aortic aneurysm repair	3
Iliac artery aneurysm	1

All pressure measurements were made at end-expiration with the patient supine using the mid-axillary line for zero reference. Thermodilution cardiac outputs were performed in triplicate using a computer (Gould Model SP-1435), averaged, and expressed per square meter of body surface area. Further calculations can be found in Appendix 1.

Nuclear Cardiac Methods

Left and right ventricular function were assessed using the equilibrium blood pool gate synchronized technique. All acquisitions were made using a small field of view mobile gamma camera with an on-board minicomputer. Red blood cells were labeled using the modified *in vivo* technique of Pavel et al.[12] Employing this technique, the patient's own red blood cells (RBCs) were pretinned by the administration of 10 μg/kg of stannous ion as stannous pyrophosphate 20 to 30 minutes prior to tagging. Actual RBC tagging was accomplished by withdrawing 3 cm^3 of blood into 20 mCi of ^{99m}Tc pertechnetate and incubating for 10 minutes *ex vivo* within a closed system.

Cardiac imaging was performed in the left anterior oblique (LAO) and right anterior oblique (RAO) projections using a high-resolution parallel hole collimator. The camera pulse height analyzer was centered at 140 kEv with a 20% window to optimize the ^{99m}Tc photopeak. The LAO projection was adjusted to attain best separation of the right and left ventricles. Data were then recorded as gate synchronized acquisition using the electrocardiogram R-wave as a physiologic trigger. The R-R interval was recorded as 28 separate frames and summated to attain a total of 200,000 counts per frame. This required an average acquisition time of 9 minutes.

Analysis of data was performed following transfer to a VAX-780* computer. Quantitative determination of ventricular function is based on the fact that at equilibrium, the measured tracer activity is proportional to volume. Therefore, if a region defining the ventricular area can be determined throughout the cardiac cycle and appropriate background contribution removed, a count volume equivalent curve of the cardiac cycle can be generated. From this curve, parameters of ventricular function, including ejection fraction, can be measured.

* Digital Equipment Corporation

TABLE 2. *Diagnoses of Patients in Hypovolemic Shock*

1. Abdominal shotgun wound
2. Ruptured abdominal aortic aneurysm (2)
3. Lower G.I. bleed
4. High intestinal fistula and third space loss after laparotomy
5. Dehydration secondary to high ileostomy output
6. Addisonian crisis

TABLE 3. *Diagnoses of Patients in Septic Shock*

1. Colon perforation, intraabdominal and pancreatic abscesses
2. Multiple small bowel perforations with peritonitis
3. Right middle lobe pneumonia
4. Perforated duodenal ulcer with peritonitis
5. Sepsis of unknown origin
6. Multiple gastric perforations and pancreatic abscess
7. Pneumonia and empyema
8. Biliary sepsis
9. Necrotizing fasciitis

There are several methods for defining the left ventricular region and generating the appropriate volume curve. We used a radial edge finding technique applied to Fourier filtered data. The correlation with contrast ventriculography at this institution has been excellent (r = 0.94). While techniques for the determination of right ventricular function from equilibrium blood pool data have been published, none has demonstrated the reproducibility of an automated system. By making slight modifications in the edge finding technique and background determinations, we have employed a similar Fourier-based system for right ventricular function determination. These determinations are highly reproducible and demonstrate excellent correlation with two accepted techniques that have been published (Hollman r = 0.95 and Maddahi r = 0.95).[13]

TABLE 4. *Data for Patients With Hypovolemic and Septic Shock Compared to Control (Mean ± SD)*

	Control N = 7	Hypovolemic Shock N = 7	Septic Shock N = 9
RVEF	0.52 ± 0.07	0.31 ± 0.05*	0.35 ± 0.16†
RVEDVI (ml/m²)	55.8 ± 7.4	106.5 ± 22*	143 ± 28*
LVEF	0.59 ± 0.18	0.60 ± 0.21	0.48 ± 0.21
LVEDVI (ml/m²)	52.3 ± 17.4	58.5 ± 16.4	107 ± 39*
CI (L/mm/m²)	2.67 ± 0.35	3.40 ± 1.19	4.59 ± 1.3‡
SVI (ml/m²)	28.8 ± 5.6	32.9 ± 10	46.8 ± 17.3†
$\overline{BP}$ (mmHg)	95.7 ± 10.5	90.3 ± 15.7	74.3 ± 14.1‡
HR (beats/min)	94.6 ± 15.7	103 ± 11	103 ± 17
$\overline{PA}$ (mmHg)	22.7 ± 6.4	26.6 ± 7.1	25.5 ± 4.8
PCWP (mmHg)	12.7 ± 3.9	13.7 ± 6.9	15.3 ± 2.5
CVP (mmHg)	15.4 ± 8	10.0 ± 5.6	12.4 ± 2.7
SVRI (dyne sec cm⁻⁵/m²)	2448 ± 470	1965 ± 638	1177 ± 440*
PVRI (dyne sec cm⁻⁵/m²)	302 ± 107	34 1± 236	234 ± 143
LVSWI (gm m/m²)	31.7 ± 2.2	34.5 ± 13.8	37.1 ± 13.3
RVSWI (gm m/m²)	3.70 ± 2.6	6.99 ± 2.5§	7.77 ± 2.5‡
Vasopressors (μg/kg/min)	0	0.71 ± 1.9	8.7 ± 9.3§
PEEP (cm H_2O)	5 ± 7.1	2.1 ± 2.7	4.2 ± 5
Age (years)	74.4 ± 9	56 ± 27	55 ± 11‡

Comparison to control significant at:
* $p < 0.001$; † $p < 0.02$; ‡ $p < 0.01$; § $p < 0.05$.

Results

Both septic and hypovolemic patients demonstrated a marked degree of RV dysfunction when compared to controls (Table 4). The average RVEF was significantly depressed in both groups of patients resuscitated from shock [Control (C) = 0.52 ± 0.07 *versus* Hypovolemia (H) = 0.31 ± 0.05 ($p < 0.001$) and Sepsis (S) = 0.35 ± 0.16 ($p < 0.02$)]. At the same time, the mean RVEDVI was significantly elevated when compared to controls [C = 55.8 ± 7.4 ml/m² *versus* H = 106.5 ± 22 ml/m² ($p < 0.001$) and S = 143 ± 28 ml/m² ($p < 0.001$)]. The control values compare favorably with the normal RVEF of 0.48 ± 0.05 using gated pool scanning,[13] demonstrating that the control patients maintained normal or above-normal RVEF in contrast to resuscitated patients. Although normal RVEDVI has been reported using thermodilution to be 90 ± 23 ml/m²,[29] this method overestimates the volume by 15% to 30% when compared to angiocardiography.[14,15] Ferlinz et al.[16] reported the RVEDVI of eight normal adults to be 76 ± 11 ml/m² (mean ± SD) using biplane angiography, which is closer to the RVEDVI of the control patients in this series. Both septic and hypovolemic patients had a significantly higher RVSWI when compared to controls, indicating an increased strain on the RV (Table 4).

There were no significant differences in LVEF between control and hypovolemic or septic patients (Table 4). Similarly, the LVEDVI of patients resuscitated from hypovolemic shock was not significantly different from controls, although those resuscitated from septic shock had a significantly greater LVEDVI [C = 52.3 ± 17.4 ml/m² *versus* H = 58.5 ± 16.4 ml/m² (NS) and S = 107 ± 39 ml/m² ($p < 0.001$)]. These values can be compared to normal values of LVEF of 0.63 ± 0.08 using gated cardiac blood pool scans.[13] Normal LVEF at this institution using gated pool scans ranges from 0.54 to 0.84, with left ventricular end-diastolic volume (not corrected for body surface area) of 52 ml to 128 ml. Kennedy et al.[17] reported a normal LVEF of 0.67 ± 0.08 and LVEDVI of 70 ± 20 ml/m² (mean ± SD) in 16 adults using biplane angiography.

There were no other significant differences in hemodynamic variables between control patients and those resuscitated from hypovolemic shock; however, patients resuscitated from septic shock had a significantly higher CI [C = 2.67 ± 0.35 L/min/m² *versus* S = 4.59 ± 1.3 L/min/m² ($p < 0.01$)], higher SVI [C

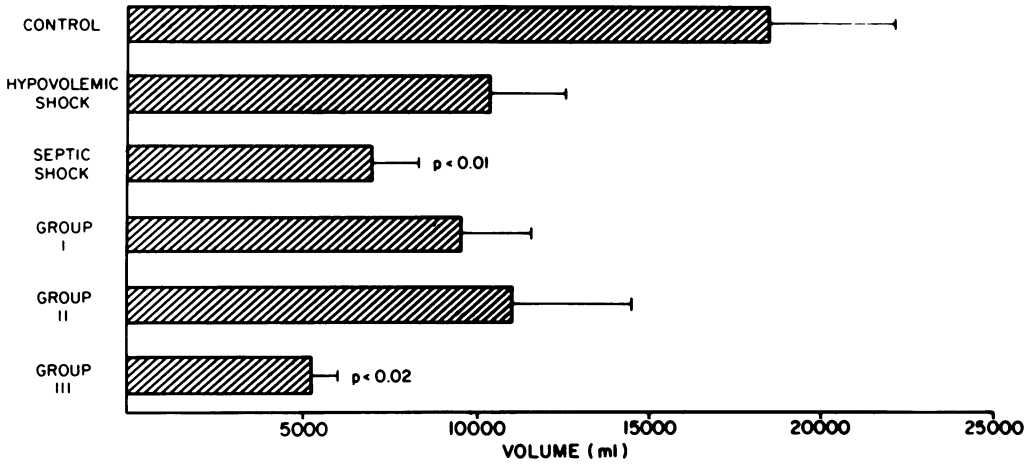

FIG. 1. Comparison of total volume of blood, crystalloid and colloid received by each group of patients in the first 24 hours after resuscitation or operation. All groups resuscitated from shock received less volume replacement than control patients.

= 28.8 ± 5.6 ml/m^2 *versus* S = 46.8 ± 17.3 ml/m^2 ($p < 0.02$)], lower $\overline{BP}$ [C = 95.7 ± 10.5 mmHg *versus* S = 74.3 ± 14.1 mmHg ($p < 0.001$), lower SVRI [C = 2448 ± 470 dyne sec cm^{-5}/m^2 *versus* S = 1177 ± 440 dyne sec cm^{-5}/m^2 ($p < 0.001$)] and were on vasopressors.

Patients resuscitated from shock were younger than control patients [C = 74 ± 9 years *versus* H = 56 ± 27 years (NS) and S = 55 ± 11 years ($p < 0.01$)] and received less volume infusion than controls (Fig. 1).

It should be noted that although the patients resuscitated from shock did not have $\overline{PA}$, CVP, or PCWP values that were significantly different from controls, all groups had elevated $\overline{PA}$ and CVP. The upper limit of normal for $\overline{PA}$ is given as 18 mmHg,[18,19] which is lower than the $\overline{PA}$ of controls (22.7 ± 6.4 mmHg), hypovolemic shock patients (26.6 ± 7.1 mmHg), and septic shock patients (25.5 ± 4.8 mmHg). The upper limit of normal right atrial pressure is 6 mmHg, which is also lower than the mean CVP in these patients (Table 4). The values for PCWP in patients in this study were close to the upper limit of normal PCWP of 12 mmHg (C = 12.7 ± 3.9 mmHg, H = 13.7 ± 6.9 mmHg, S = 15.3 ± 2.5 mmHg). PVRI was elevated in most of the patients according to the average normal value reported by Holmgren et al.[18] of 125 dyne sec cm^{-5}. A lower average normal value was reported by Barratt-Boyes et al.[19] of 67 ± 23 dyne sec cm^{-5}. Higher PVRI values were calculated in nearly all patients in this study (C = 302 ± 107 dyne sec cm^{-5}/m^2, H = 341 ± 236 dyne sec cm^{-5}/m^2 and S = 234 ± 143 dyne sec cm^{-5}/m^2).

The patients resuscitated from shock can be regrouped on the basis of right and left heart performance into three groups (Table 5). Group I (RVEF < 0.40 and LVEF > 0.40) consisted of eight patients (five hypovolemic, three septic) who had significantly depressed RVEF [C = 0.52 ± 0.07 *versus* 0.30 ± 0.05 ($p < 0.001$)] and elevated RVEDVI [C = 55.8 ± 7.4 ml/m^2 *versus* 129.2 ± 32.7 ml/m^2 ($p < 0.001$)] with normal LV function (LVEF 0.63 ± 0.15 and LVEDVI 63.6 ± 21.3 ml/m^2, neither different from controls). Group II (RVEF > 0.40 and LVEF > 0.40) consisted of three patients

TABLE 5. *Data for Groups I (RVEF <0.40 and LVEF >0.40), Group II (RVEF >0.40 and LVEF > 0.40), and Group III (RVEF <0.40 and LVEF <0.40) Compared to Controls (Mean ± SD)*

	Control N = 7	Group I N = 8	Group II N = 3	Group III N = 5
RVEF	0.52 ± 0.07	0.30 ± 0.06*	0.54 ± 0.06	0.25 ± 0.06*
RVEDVI (ml/m^2)	55.8 ± 7.4	129.2 ± 32.7*	121.1 ± 22*	127.1 ± 40.4*
LVEF	0.59 ± 0.18	0.63 ± 0.15	0.67 ± 0.20	0.29 ± 0.04‡
LVEDVI (ml/m^2)	52.3 ± 17.4	63.6 ± 21.3	107.2 ± 45.2†	108.6 ± 44.3†
CI (L/min/m^2)	2.67 ± 0.35	3.92 ± 1.04‡	6.03 ± 0.81*	3.14 ± 0.77
SVI (ml/m^2)	28.8 ± 5.6	37.5 ± 7.6§	66.1 ± 17*	30.7 ± 8.3
$\overline{BP}$ (mmHg)	95.7 ± 10.5	83.4 ± 18.8	69 ± 6.1‡	85.3 ± 15.7
HR (beats/min)	94.6 ± 15.7	104 ± 10	98 ± 20.6	104 ± 18
$\overline{PA}$ (mmHg)	22.7 ± 6.4	25 ± 5.8	22.9 ± 3.4	29.5 ± 5.7
PCWP (mmHg)	12.7 ± 3.9	15.8 ± 5.2	15.3 ± 2.3	12.4 ± 5.2
CVP (mmHg)	15.4 ± 8	11.6 ± 4	13.3 ± 4.2	9.8 ± 5
SVRI (dyne sec cm^{-5}/m^2)	2448 ± 470	1558 ± 630†	750 ± 139*	1928 ± 500
PVRI (dyne sec cm^{-5}/m^2)	302 ± 107	211 ± 80	102 ± 39†	500 ± 175§
LVSWI (gm m/m^2)	31.7 ± 2.2	34.8 ± 13.2	47.8 ± 10.4‡	30.7 ± 11.9
RVSWI (gm m/m^2)	3.70 ± 2.6	6.85 ± 2.1§	8.62 ± 4.3§	7.63 ± 1.8†
Vasopressors (μg/kg/min)	0	2.5 ± 4.6	11 ± 9.6†	6 ± 10.8
PEEP (cmH_2O)	5 ± 7.1	2.5 ± 2.7	7.7 ± 7.5	2 ± 2.7
Age (years)	74.4 ± 9	52.8 ± 24§	60.3 ± 5§	56.8 ± 15§

Comparison to control significant at:
* $p < 0.001$; † $p < 0.02$; ‡ $p < 0.01$; § $p < 0.05$.

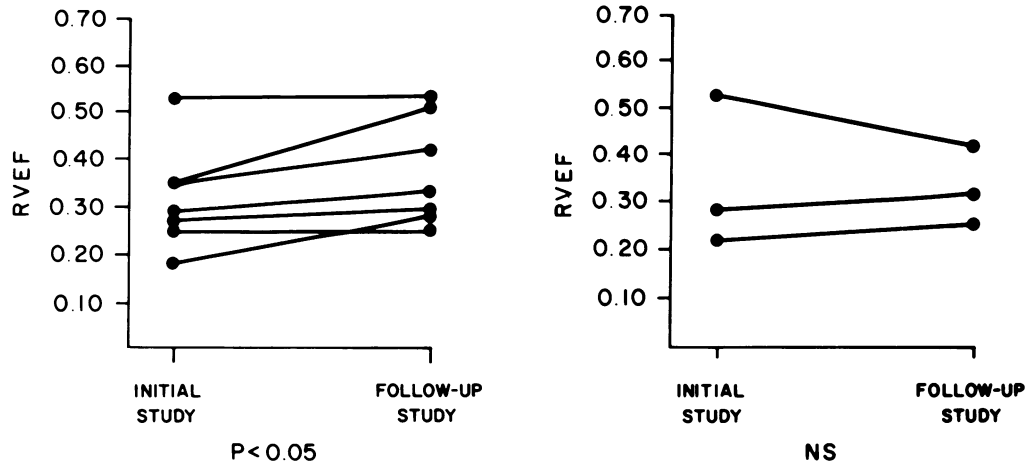

FIG. 2. Individual changes in RVEF for group showing clinical improvement (left) and the group showing clinical deterioration (right). There was a significant increase in RVEF for the group showing clinical improvement.

(all septic) with fairly normal RVEF (0.54 ± 0.06) and LVEF (0.67 ± 0.20) but elevated RVEDVI [C = 55.8 ± 7.4 ml/m^2 *versus* 121.1 ± 22 ml/m^2 ($p < 0.001$)] and LVEDVI [C = 52.3 ± 17.4 ml/m^2 *versus* 107.2 ± 45.2 ml/m^2 ($p < 0.02$)]. Group III (RVEF < 0.40 and LVEF < 0.40) consisted of five patients (two hypovolemic, three septic) who had biventricular depression of function with low RVEF [C = 0.52 ± 0.07 *versus* 0.25 ± 0.06 ($p < 0.001$)], low LVEF [C = 0.59 ± 0.18 *versus* 0.29 ± 0.04 ($p < 0.01$)], high RVEDVI [C = 55.8 ± 7.4 ml/m^2 *versus* 127.1 ± 40.4 ml/m^2 ($p < 0.001$)] and high LVEDVI [C = 52.3 ± 17.4 ml/m^2 *versus* 108.6 ± 44.3 ml/m^2 ($p < 0.02$)].

This re-grouping of patients had important implications for either improvement or deterioration and death. Three of the five patients in group III had follow-up studies which showed the RVEF to remain below 0.40 [initially 0.23 ± 0.05 *versus* 0.29 ± 0.03 on follow-up (NS)] but the LVEF increased to above 0.40 [0.31 ± 0.02 initially *versus* 0.45 ± 0.05 on follow-up (NS)]. Although these patients would meet the criteria for group I due to some recovery of left ventricular function, they still had a high mortality rate (67%).

The patients who had follow-up studies were then grouped as to improvement (N = 7: three hypovolemic and four septic; five group I, one group II, and one group III) or deterioration (N = 3: two hypovolemic and one septic; one group II and two group III). Patients who improved showed a significant increase in RVEF [from 0.32 ± 0.11 to 0.37 ± 0.11 ($p < 0.05$)] (Fig. 2) and a decrease in RVEDVI [from 127 ± 28 ml/m^2 to 78 ± 12 ml/m^2 ($p < 0.01$)] (Fig. 3). The CI and SVI of these patients also decreased to values that were nearer control levels. CI decreased from 3.93 ± 0.99/min/m^2 to 2.99 ± 0.71 L/min/m^2 ($p < 0.02$) and SVI decreased from 38.3 ± 8.3 ml/m^2 to 28.3 ± 6.4 ml/m^2 ($p < 0.02$). In contrast, the only significant difference between initial and follow-up studies for patients who showed clinical deterioration was an increase in RVEDVI [from 87 ± 19 ml/m^2 to 124 ± 20 ml/m^2 ($p < 0.01$)]. There were

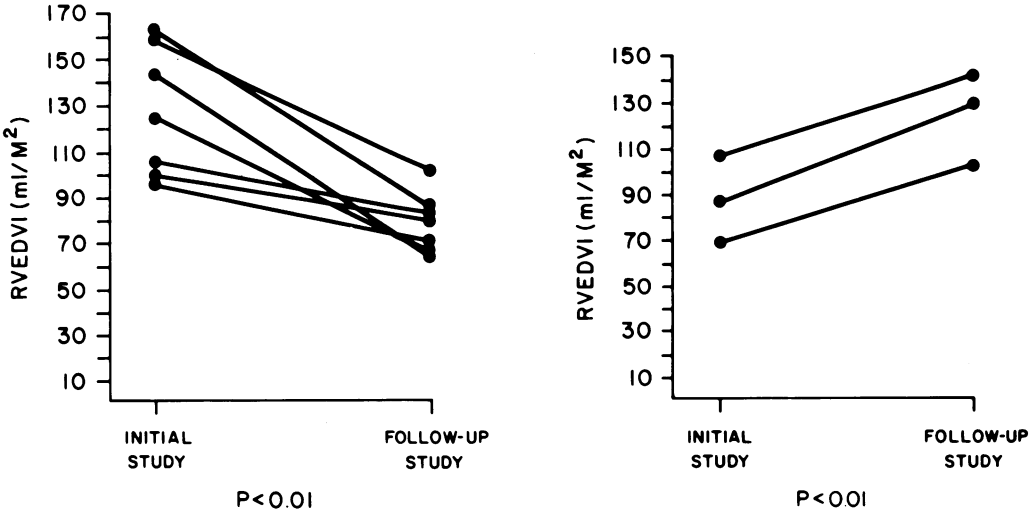

FIG. 3. Individual changes in RVEDVI for groups showing clinical improvement (left) and clinical deterioration (right). Note the significant decrease in RVEDVI for the group showing clinical improvement and the significant increase in RVEDVI for the group showing clinical deterioration.

no significant differences in LVEF or LVEDVI for the groups showing either improvement or deterioration. When comparing the initial study of the patients showing clinical improvement to that of the patients showing clinical deterioration, the only significant difference was a higher PVRI in patients who deteriorated [226 ± 120 dyne sec cm^{-5}/m^2 *versus* 516 ± 280 dyne sec cm^{-5}/m^2 ($p < 0.05$)].

The overall mortality rate among the patients who had been resuscitated from shock was 56% (nine out of 16). For patients resuscitated from hypovolemic shock, there was a 43% mortality rate (three of seven) compared to a 67% mortality rate (six of nine) in patients resuscitated from septic shock. When the patients were grouped according to ejection fractions, group I (RVEF < 0.40 and LVEF > 0.40) had a mortality rate of 25% (two of eight), group II (RVEF > 0.40 and LVEF > 0.40) had a mortality rate of 100% (three of three), and group III (RVEF < 0.40 and LVEF < 0.40) had an 80% mortality rate (four of five). The mortality rate for group I was significantly less than that of group II and group III combined ($p = 0.02$, Fisher's Exact Test). Of the three patients who showed clinical deterioration on follow-up study, all died. Of the patients who showed initial improvement, one subsequently deteriorated, and a second follow-up study showed decreased RV function. She died and was included with the patients who showed clinical deterioration.

The patients resuscitated from shock were then grouped into survivors (N = 7) or non-survivors (N = 9). There were no significant differences in any of the measurements in the initial study that would have distinguished survivors from non-survivors (Table 6). Comparing the follow-up studies of survivors (N = 6) *versus* non-survivors (N = 3) showed that non-survivors had significantly larger RVEDVI, larger SVI, and greater RVSWI. Comparison of survivors' initial study to survivors' follow-up (N = 6) study showed a significant reduction in RVEDVI from 133.9 ± 25.1 ml/m^2 to 79.7 ± 12.7 ml/m^2 ($p < 0.001$) and an increased RVEF that was significant using the paired t-test [from 0.29 ± 0.06 to 0.35 ± 0.10 ($p < 0.05$ for paired t-test)]. There was also a significant reduction in SVI [from 38.1 ± 7.8 ml/m^2 to 27.0 ± 5.7 ml/m^2 ($p < 0.02$)].

Comparing initial to follow-up studies in non-survivors (N = 3) showed no significant differences in any of the measurements (Table 6). There were no significant differences between survivors and non-survivors in terms of age [51.6 ± 25.4 years *versus* 58.4 ± 12.1 years (NS)], total time hypotensive [97 ± 24 minutes *versus* 162 ± 117 minutes (NS)], or total volume of fluid administered in the first 24 hours after resuscitation [9000 ± 6350 ml *versus* 8240 ± 4370 ml (NS)].

Using data from all studies (N = 34), no significant correlations were found between PCWP and LVEDVI [r = −0.13 (NS)] (Fig. 4) or between CVP and RVEDVI [r = −0.22 (NS)] (Fig. 5), indicating, as others have observed,[1,3,4,6,7] that filling pressures cannot be used to predict ventricular end-diastolic volumes. In addition, there were no significant correlations between $\overline{PA}$ and RVEDVI (r = 0.04, NS) or between PVRI and RVEDVI (r = −0.10, NS). There was a significant negative correlation noted between RVEF and PVRI (r = −0.34, $p < 0.05$) (Fig. 6). PCWP and CVP were not significantly related to SVI or CI. In contrast, both LVEDVI and RVEDVI were significantly correlated with CI (Fig. 7) (r = 0.49, $p < 0.01$ for LVEDVI and r = 0.48, $p < 0.01$ for RVEDVI) and with SVI (r = 0.59, $p < 0.01$ for LVEDVI and r = 0.51, $p < 0.01$ for RVEDVI). In addition, a significant positive correlation was noted between RVEDVI and LVEDVI (Fig. 8) (r = 0.63, p

TABLE 6. *Data for Survivors and Nonsurvivors as Compared to Controls (Mean ± SD)*

	Survivors Initial N = 7	Nonsurvivors Initial N = 9	Survivors Follow-up N = 6	Nonsurvivors Follow-up N = 3
RVEF	0.29 ± 0.06	0.36 ± 0.15	0.35 ± 0.10‡	0.34 ± 0.07
RVEDVI (ml/m^2)	133.9 ± 25.1	121.6 ± 36.7	79.7 ± 12.7*	133.2 ± 33.8§
LVEF	0.59 ± 0.17	0.49 ± 0.24	0.56 ± 0.14	0.63 ± 0.22
LVEDVI (ml/m^2)	69.1 ± 20.3	98.8 ± 46.1	50.6 ± 15.7	75.5 ± 26.5
CI (l/min/m^2)	4.00 ± 1.10	4.13 ± 1.58	2.85 ± 0.67‡	3.79 ± 0.68
SVI (ml/m^2)	38.1 ± 7.8	42.8 ± 20.3	27.0 ± 5.7†	43.7 ± 4.8§
$\overline{BP}$ (mmHg)	87.0 ± 15.2	78.3 ± 16.7	88.0 ± 20	75.3 ± 16.3
HR (beats/min)	104 ± 10	102 ± 17	107 ± 21	86.3 ± 12
$\overline{PA}$ (mmHg)	25.3 ± 7.2	26.5 ± 5.1	24 ± 6.7	31.4 ± 4
PCWP (mmHg)	15.3 ± 3.9	14.1 ± 5.6	12.8 ± 5.1	18.7 ± 15.6
CVP (mmHg)	11.3 ± 3.3	11.4 ± 5.1	10.1 ± 3.9	12 ± 7.5
SVRI (dyne sec cm^{-5}/m^2)	1630 ± 630	1440 ± 700	2250 ± 670	1470 ± 750
PVRI (dyne sec cm^{-5}/m^2)	232 ± 118	319 ± 230	318 ± 125	300 ± 300
LVSWI (gm m/m^2)	37.3 ± 12.1	34.9 ± 12.8	29.0 ± 14.2	34.9 ± 15.7
RVSWI (gm m/m^2)	7.16 ± 2.18	7.63 ± 2.72	5.09 ± 1.83	10.9 ± 2.25§
Vasopressors (μg/kg/min)	1.0 ± 1.9	8.4 ± 9.5	0.7 ± 1.6	8.3 ± 10.4
PEEP (cmH_2O)	1.4 ± 2.4	4.8 ± 4.8	1.7 ± 2.6	3.3 ± 2.9
Age (years)	51.6 ± 25.4	58.4 ± 12.1	—	—
Total time hypotensive (minutes)	97 ± 24	162 ± 117	—	—
Total volume in first 24 hrs	9000 ± 6350	8240 ± 4370	—	—

Comparison to initial study at:
* $p < 0.001$; † $p < 0.02$; ‡ $p < 0.05$.
§ Comparison to survivors' follow-up study at $p < 0.01$.

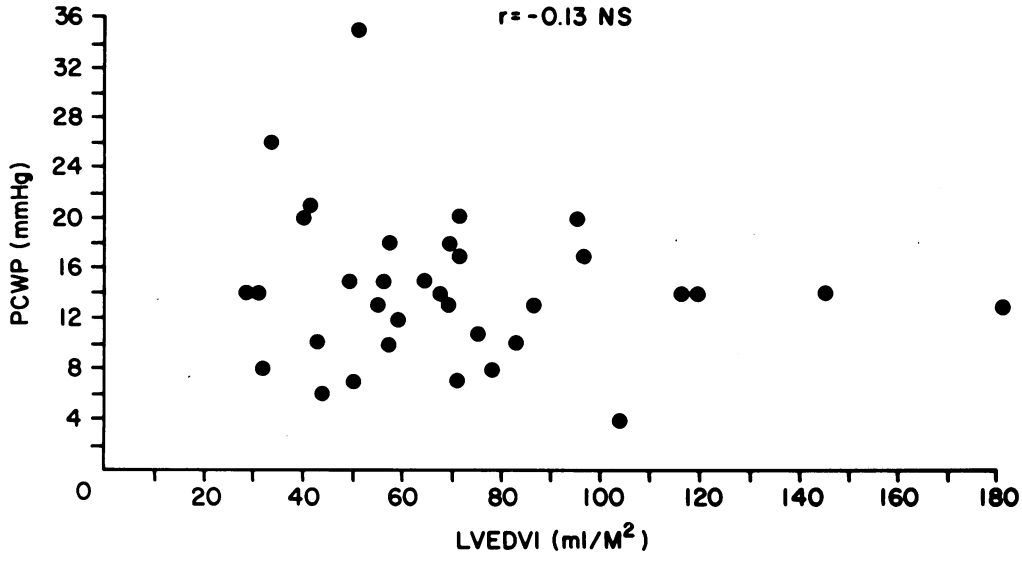

FIG. 4. No significant correlation was observed between PCWP and LVEDVI using data from all studies.

< 0.001), but the regression equation showed that the LVEDVI increased only slightly more than half of any increase in RVEDVI.

Discussion

The failure of some critically ill patients to respond predictably to volume loading can be explained in part by the observations of Calvin et al.[4] who found that PCWP did not accurately reflect changes in left ventricular preload and that 80% of the variance in the PCWP could be explained on the basis of changes in CVP and right ventricular end-diastolic volumes. LVEDV was found to depend on right ventricular function and pulmonary vascular resistance. In patients with a beneficial response to volume loading, either an increase in LVEDV or LVEF was seen which did not correlate with PCWP. The patients who failed to respond to volume infusion all demonstrated a significant increase in PCWP with no change in LVEDV, which suggested an acute change in left ventricular compliance. These patients had evidence of depressed LV function with diminished stroke volume index. The systemic vascular resistance index (SVRI) was elevated, but there was no change in dv/dt, suggesting no reduction in contractility. An increased CVP in these patients suggested that changes in RV loading may have changed LV compliance and function.

Glanz et al.[6] have shown that the RV exerts an external load on the LV within an intact pericardium and can alter LV distensibility. Several other studies have also demonstrated that elevated RVEDV can compromise LV function.[7,10,11,20]

Salisbury[21] demonstrated RV dilatation and failure in dogs with progressive pulmonary artery occlusion that

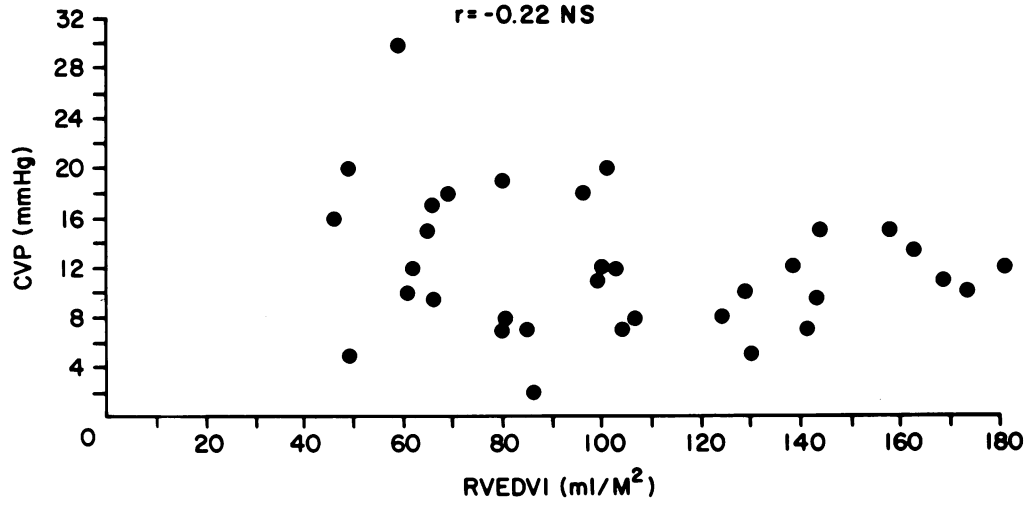

FIG. 5. No significant correlation between CVP and RVEDVI was observed using data from all studies. Filling pressures cannot be used to predict end-diastolic volumes in either ventricle.

was corrected when right coronary artery flow was restored by raising aortic diastolic pressure. Fineberg et al.[22] also showed that the RV responded poorly to an increase in afterload, especially when coronary blood flow was reduced by lower systemic arterial pressure. As pointed out by Martyn et al.[8] the increased oxygen requirement resulting from increased wall stress in a dilated ventricle may not be satisfied when coronary blood flow is decreased secondary to hypotension and tachycardia, and a vicious cycle of RV dilatation and failure may occur.

A significant degree of RV dysfunction was observed in this study of patients resuscitated from hypovolemic and septic shock, when compared to controls who received a large amount of volume replacement during elective surgery without hypotension. This observation is even more significant, because the control patients were generally older and received more fluid replacement. Although RV dysfunction was associated with pulmonary hypertension and an elevation of PVRI when compared to normals, the degree of dysfunction did not correlate with either of these variables, except for the correlation between RVEF and PVRI. In addition, control patients also developed increased PVRI, but did not develop RV dysfunction. There was no difference in the degree of pulmonary hypertension among the different groups of patients resuscitated from shock. Although there was a statistically significant elevation of PVRI initially in patients who showed clinical deterioration, there was also a small but significant increase in PVRI in the follow-up study of patients showing improvement.

Pulmonary hypertension and increased PVRI have been reported after burn injury,[9] acute pulmonary injury,[23] experimental hemorrhagic shock,[24] and sepsis.[25] Any of these may be accompanied by RV dysfunction, but only Martyn et al.[9] measured RV ejection fraction and end-diastolic volume. Ventricular function in the other reports was assessed by filling pressures, stroke work index, mean systolic ejection rate, or a combination of these which do not provide information on ejection fraction or end-diastolic volume.

Although pulmonary hypertension and increased PVRI may be important in the development of RV dysfunction, they do not appear to be the sole determinants. In considering other factors, the most obvious difference between the control patients and those resuscitated from shock was the hypotensive insult. It has been shown that RV dysfunction produced by progressive pulmonary artery constriction can be corrected by increasing coronary blood flow.[21,26] Fineberg et al.[22] also demonstrated the vulnerability of the stressed RV to diminished coronary blood flow. These data suggest that the decreased

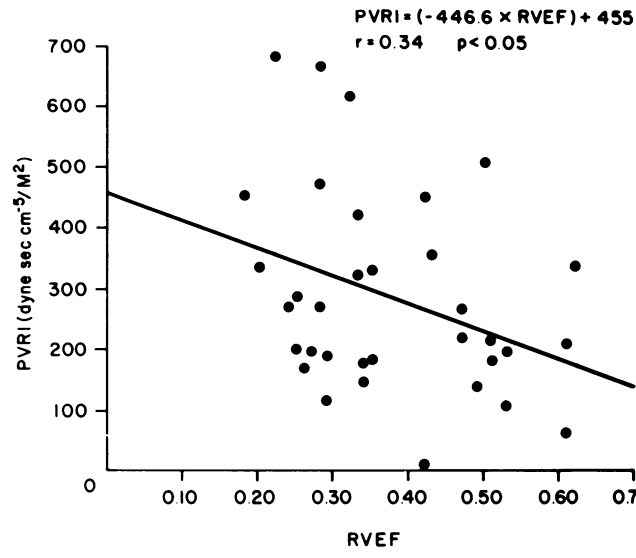

FIG. 6. A significant negative correlation was observed between PVRI and RVEF, suggesting that the PVRI does have a significant effect on RV function.

coronary blood flow accompanying shock may make the RV vulnerable to the acute pressure and flow load that is placed on it during fluid resuscitation.[27] The RV of patients who do not have reduced coronary blood flow is apparently better able to adjust to acute increases in flow and afterload. Gold et al.[28] showed that pulmonary artery occlusion, sufficient to increase RVEDP and decrease aortic pressure, selectively decreased coronary blood flow to the right ventricular subendocardium even when coronary vasodilator reserve, as measured after adenosine infusion, was not exhausted. Other authors have observed that if coronary blood flow is maintained during shock, there is less depression of myocardial function.[29-31] A significant reduction in subendocardial blood flow has been observed in both hemorrhagic[32] and septic shock[27] and is thought to contribute to myocardial dysfunction. Our data support this hypothesis and suggest that the acute pressure and flow load imposed by resuscitation can exacerbate the subendocardial ischemia by increasing the oxygen requirements of the RV myocardium due to the increased wall stress of a dilated ventricle by the Laplace relationship.[33] An increase in RV oxygen requirements is supported further by the observation of significantly increased RVSWI in all patients resuscitated from shock compared to controls (Table 5). Ostern et al.[34] also observed increased RVSWI in a group of non-surviving trauma patients and Zapol et al.[35] documented markedly increased RVSWI in a group of patients with acute respiratory failure. They postulated that the increased workload imposed on the RV by increased PVRI might be a factor limiting sur-

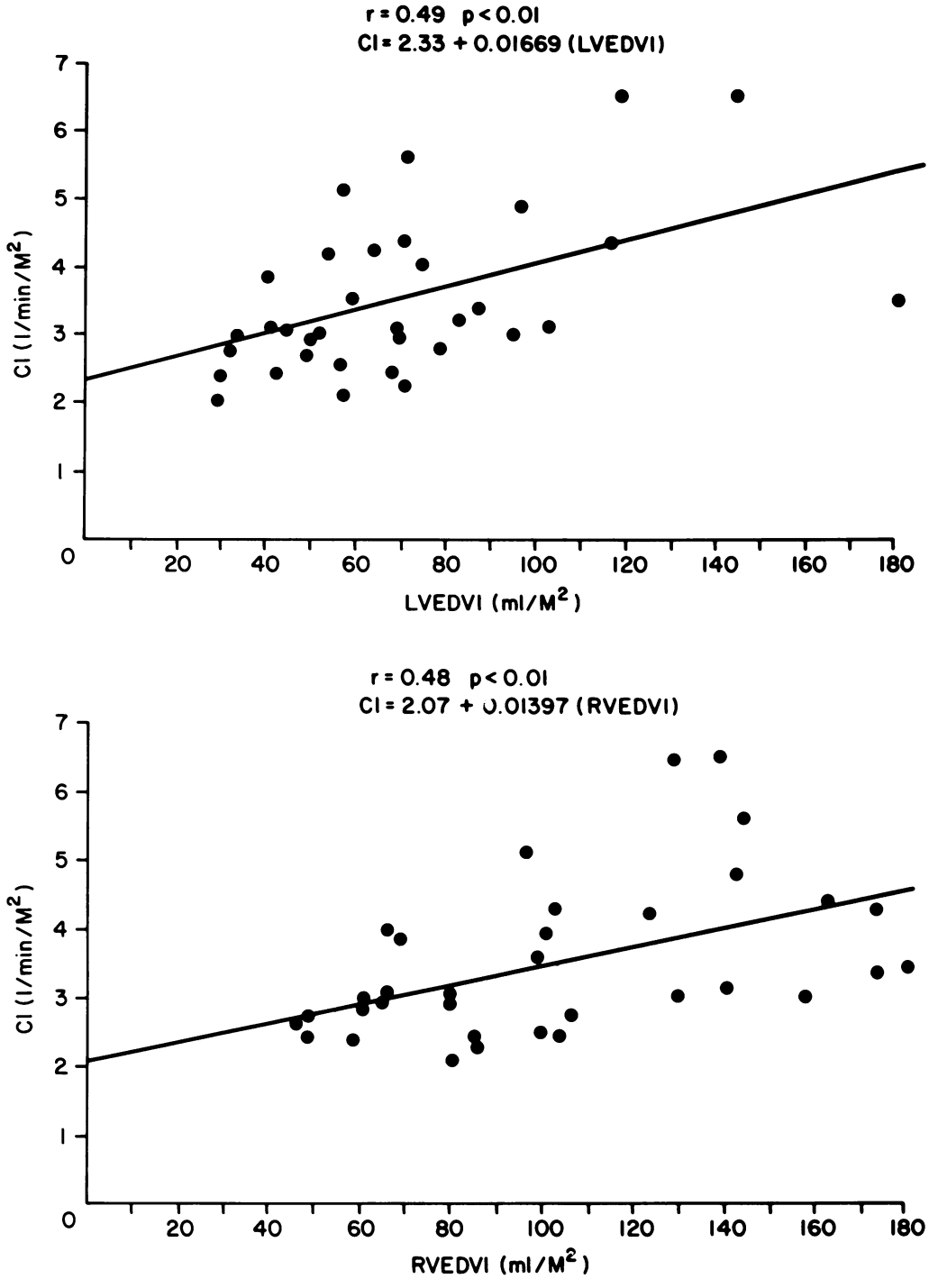

FIG. 7. A significant positive correlation was observed between LVEDVI and CI and RVEDVI and CI, which is consistent with the Frank-Starling principle.

vival. In addition to reduced coronary blood flow, the elaboration of myocardial depressant factors[36] may contribute to ventricular dysfunction. In the present report, patients who showed improvement in RV function (increased RVEF and decreased RVEDVI) also improved clinically and survived. On the other hand, patients who showed deterioration in RV function showed clinical deterioration, suggesting that RV failure played a major role in determining the clinical course.

Since the decrease in coronary blood flow during shock also affects the left ventricle, it is not surprising that some patients resuscitated from shock also demonstrated LV dysfunction. However, as opposed to the uniform incidence of RV dysfunction, there was only

a 50% incidence of LV dysfunction in this same group (eight patients in group II and group III). However, in the three patients in group III who had follow-up studies, despite improvement in LV function, further deterioration in RV function in two of them was followed by death. In the remaining patient, simultaneous improvement in RV and LV function allowed survival. Therefore, although LV dysfunction does occur after resuscitation from shock, it appears to be more transient and less critical to survival.

The RV dilatation observed in the resuscitated patients raises the possibility of LV compression due to RV-LV interaction within an intact pericardium, as shown by others.[6,7,10] When the RV dilates, it can encroach on the LV through leftward shift of the interventricular septum and reduce LV filling volume. This can result in a rise in left ventricular filling pressure and a fall in output that may be compensated by an increased ejection fraction. This clinical picture suggests LV failure, unless ventricular volumes are measured to discover a failing right ventricle. The patients in group I may support this concept, since they all demonstrated depressed RVEF with elevated RVEDVI but normal LVEF and LVEDVI. In general, however, there was a positive correlation between RVEDVI and LVEDVI, suggesting more uniform response to loading than encroachment (Fig. 8).

There was no correlation between filling pressures and end-diastolic volumes, cardiac index, or stroke volume indexes, as shown by others.[1,2,4,8] This may contribute to the ventricular dysfunction observed by allowing overtransfusion when filling pressures are used to guide resuscitation. On the other hand, both RVEDVI and LVEDVI correlated positively with CI and SVI and would seem to be more appropriate guidelines for resuscitation.

In summary, we have observed RV dysfunction as measured by decreased RVEF and increased RVEDVI in patients resuscitated from hypovolemic and septic shock. This RV dysfunction could not be attributed to an increased PVRI, since control patients with similar elevated PVRI did not develop RV dysfunction. Most likely, dysfunction results from reduced coronary perfusion, especially to the RV subendocardium during shock in combination with an acute pressure-volume load during rapid fluid resuscitation. The resultant RV dilatation with increased oxygen demand due to increased wall tension may not be satisfied by the coronary circulation in the presence of elevated right-sided pressures. The LV is also susceptible to dysfunction after resuscitation, but it appears to be more transient and of less clinical significance. An improvement in RV

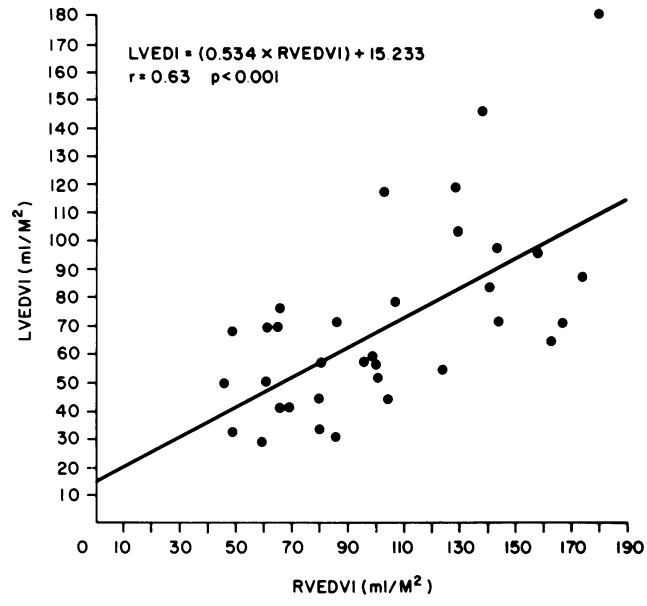

FIG. 8. A significant positive correlation was observed between LVEDVI and RVEDVI; however, according to the regression equation, the LVEDVI increased only a little more than half of any increase in RVEDVI.

function (increased RVEF and decreased RVEDVI) was associated with survival, whereas deterioration (decreased RVEF and increased RVEDVI) was associated with death. The initial degree of RV dysfunction was not predictive of the clinical course which correlated only with follow-up studies showing either improvement or deterioration in RV function. There was no significant difference in either LVEF or LVEDVI between patients who survived or died and no correlations were found between filling pressures and ventricular volumes or ejection fractions. Therefore, reliance on ventricular filling pressures for resuscitation in both hypovolemic and septic shock is not sufficient to prevent RV overload and dysfunction which correlate with mortality. Bedside measurement of RV performance may allow earlier intervention to correct dysfunction and adds an important dimension to the care of the patient resuscitated from shock.

References

1. Ellis RJ, Mangano DT, Van Dyke DC. Relationship of wedge pressure to end-diastolic volume in patients undergoing myocardial revascularization. J Thorac Cardiovasc Surg 1979; 78:605–613.
2. Baek S, Makabali GG, Bryan-Brown CW, et al. Plasma expansion in surgical patients with high central venous pressure (CVP); the relationship of blood volume to hematocrit, CVP, pulmonary wedge pressure and cardiorespiratory changes. Surgery 1975; 78:304–315.
3. Alderman EL, Glantz SA. Acute hemodynamic interventions shift

the diastolic pressure-volume curve in man. Circulation 1976; 54:662–671.
4. Calvin JE, Driedger AA, Sibbald WJ. The hemodynamic effect of rapid fluid infusion in critically ill patients. Surgery 1981; 90:71–76.
5. Sarnoff SJ, Berglund E. Ventricular function. I. Starling's law of the heart, studied by means of simultaneous right and left ventricular function curves in the dog. Circulation 1953; 9:706–718.
6. Glantz SA, Parmley WW. Factors which affect the diastolic pressure-volume curve. Circ Res 1978; 42:171–180.
7. Ross J. Acute displacement of the diastolic pressure-volume curve of the left ventricle: role of the pericardium and the right ventricle. Circulation 1979; 59:32–37.
8. Martyn JAJ, Snider MT, Farago LF, Burke JF. Thermodilution right ventricular volume: a novel and better predictor of volume replacement in acute thermal injury. J Trauma 1981; 21:619–626.
9. Martyn JAJ, Snider MT, Szyfelbein SK, et al. Right ventricular dysfunction in acute thermal injury. Ann Surg 1980; 191:330–335.
10. Shirato K, Shabetai R, Bhargava V, et al. Alteration of the left ventricular diastolic pressure-segment length relation produced by the pericardium: effects of cardiac distension and afterload reduction in conscious dogs. Circulation 1978; 57:1191–1198.
11. Ludbrook PA, Byrne JD, McKnight RC. Influence of right ventricular hemodynamics on left ventricular diastolic pressure-volume relations in man. Circulation 1979; 59:21–31.
12. Pavel DG, Zimmer AM, Patterson VN. In vivo labeling of red blood cells with 99mTc: A new approach to blood pool visualization. J Nucl Med 1977; 18:305–308.
13. Maddahi J, Berman DS, Matsuoka DT. A new technique for assessing right ventricular ejection fraction using rapid multiple-gated equilibrium cardiac blood pool scintigraphy. Circulation 1979; 60:681–589.
14. Rapaport E. Usefulness and limitations of thermal washout technics in ventricular volume measurement. Am J Cardiol 1966; 18:226–234.
15. Bartle SH, Sanmarco ME. Comparison of angiocardiographic and thermal washout technics for left ventricular volume measurement. Am J Cardiol 1966; 18:235–252.
16. Ferlinz J, Gorlin R, Cohn PF, et al. Right ventricular performance in patients with coronary artery disease. Circulation 1975; 52:608.
17. Kennedy JW, Baxley WA, Figley MM, et al. Quantitative angiocardiography. I. The normal left ventricle in man. Circulation 1966; 34:272.
18. Holmgren A, Jonsson B, Sjöstrand T. Circulatory data in normal subjects at rest and during exercise in recumbent position, with special reference to the stroke volume at different work intensities. Acta Physiol Scand 1960; 49:343–363.
19. Barratt-Boyes BG, Wood EH. Cardiac output and related measurements and pressure values in the right heart and associated vessels, together with an analysis of the hemodynamic response to the inhalation of high oxygen mixtures in healthy subjects. J Lab Clin Med 1958; 51:72–90.
20. Maruyama Y, Ashikawa K, Isoyama S, et al. Mechanical interactions between four heart chambers with and without the pericardium in canine hearts. Circ Res 1982; 50:86–100.
21. Salisbury PF. Coronary artery pressure and strength of right ventricular contraction. Circ Res 1955; 3:633.
22. Fineberg MH, Wiggers CJ. Compensation and failure of the right ventricle. Am Heart J 1936; 11:255.
23. Powers SR, Shah D, Ryon D, et al. Hypertonic mannitol in the therapy of the acute respiratory distress syndrome. Ann Surg 1977; 185:619–625.
24. Eaton RM. Pulmonary edema. Experimental observations on dogs following acute peripheral blood loss. J Thorac Surg 1947; 16:668.
25. Clowes GHA Jr, Farrington GH, Zuschneid W, et al. Circulating factors in the etiology of pulmonary insufficiency and right heart failure accompanying severe sepsis. Ann Surg 1970; 171:663–678.
26. Brooks H, Kirk ES, Vokonas PS, et al. Performance of the right ventricle under stress: relation to right coronary flow. J Clin Invest 1971; 50:2176–2183.
27. Kleinman WM, Krause SM, Hess ML. Differential subendocardial perfusion and injury during the course of gram-negative endotoxemia. Adv Shock Res 1980; 4:139–152.
28. Gold FL, Bache RJ. Transmural right ventricular blood flow during acute pulmonary artery hypertension in the sedated dog. Evidence for superdocardial ischemia despite residual vasodilator reserve. Circ Res 1982; 51:196–204.
29. Rapaport E, Wang M, Ferguson R, et al. Right ventricular volumes in patients with and without heart failure. Circulation 1965; 41:531.
30. Elkins RC, McCurdy JR, Brown PP, Greenfield LJ. Effects of coronary perfusion pressure on myocardial performance during endotoxin shock. Surg Gynecol Obstet 1973; 137:991–996.
31. Daniell HB. Coronary flow alterations on myocardial contractility, oxygen extraction and oxygen consumption. Am J Physiol 1973; 225:1020.
32. Carlson EL, Selinger SL, Utley J, Hoffman JIE. Intramyocardial distribution of blood flow in hemorrhagic shock in anesthetized dogs. Am J Physiol 1976; 230:41–49.
33. Gorlin R. Recent conceptual advances in congestive heart failure. JAMA 1962; 179:441.
34. Oestern JH, Trentz O, Kolbow H, et al. Early cardiorespiratory prognostic patterns in multiple trauma patients. Adv Shock Res 1979; 2:43–53.
35. Zapol WM, Snider MT. Pulmonary hypertension in severe acute respiratory failure. N Engl J Med 1977; 296:476.
36. Lefer AM. Properties of cardioinhibitory factors produced in shock. Fed Proc 1978; 37:2734.

Appendix 1

1. Systemic and pulmonary vascular resistances:

$$SVRI = \frac{\overline{BP} - CVP}{CI} \times 80;$$

$$PVRI = \frac{\overline{PA} - PCWP}{CI} \times 80.$$

where

SVRI = systemic vascular resistance index (dynes sec cm^{-5})/m^2;
PVRI = pulmonary vascular resistance index (dynes sec cm^{-5})/m^2;
$\overline{BP}$ = mean blood pressure (diastolic + 1/3 systolic-diastolic) (mmHg);
CVP = central venous pressure (mmHg);
PCWP = pulmonary capillary wedge pressure (mmHg),
CI = cardiac index (L/min/m^2).

2. Stroke volume index = $SVI = \frac{CI}{HR} \times 1000$ (ml/beat/m^2).

3. Left and right ventricular stroke work index:

$$LVSWI = SVI \times (\overline{BP} - PCWP) \times 0.0136 \text{ (g-m/m}^2\text{)};$$

$$RVSWI = SVI \times (\overline{PA} - CVP) \times 0.036 \text{ (g-m/m}^2\text{)}.$$

4. Left and right ventricular end-diastolic volume index:

$$LVEDVI = \frac{SVI}{LVEF} \text{ (ml/m}^2\text{)};$$

$$RVEDVI = \frac{SVI}{RVEF} \text{ (ml/m}^2\text{)}.$$

Discussion

DR. LOUIS R. M. DEL GUERCIO (Valhalla, New York): As Dr. Greenfield pointed out, the preload factor in the original Starling-Frank hypothesis had nothing to do with pressure. It was a volume load, and the stretch of the muscle fibers then was related to the subsequent work during systole.

But we compromise, and as biomedical engineers and physiologists in clinical settings, we have a tendency to measure the things that we *can* rather than the things that we *should;* and this is why, over the past many years, we have been measuring filling pressures, first the central venous side, and subsequently, with the advent of the Swan-Ganz catheter, the left side of the heart.

We have noted that the right side of the heart is particularly vulnerable to increases in pressure work. It handles increased volume loads very handily, but in such situations as pulmonary embolism or acute respiratory distress syndromes, the right ventricle is more vulnerable than the left, particularly in young individuals.

We have tended to concentrate on what is happening in the left side of the heart, primarily because we have used the Swan-Ganz catheter for monitoring elderly patients, patients with known arteriosclerotic cardiovascular disease; but in the acute trauma setting and in the acute setting related to massive resuscitation in young people, it is the right side of the heart, as has been shown by Dr. Greenfield, that is very likely to fail. This may be related to the geometry of the ventricle, as he has demonstrated.

We too have found this phenomenon, and are searching for techniques to measure ejection fractions, which, after all, goes all the way back to the original Starling-Frank hypothesis. Our only hope is that modern technology will enable us to achieve this sort of monitoring with a technique that can be easily applied to the bedside in the clinical shock setting.

DR. WATTS R. WEBB (New Orleans, Louisiana): Our own work, both in hypervolemia and in septic shock, both clinically and experimentally, demonstrates, we feel, that there is virtually always a marked increase in pulmonary artery pressure, and, similarly, in pulmonary artery resistance, which was alluded to by Dr. Greenfield here. It is not related to the wedge pressure at all, but I think that the flow and the amount of resistance are the things that are the most important.

I think that the increased volume, which is here characterized as a dysfunction, may be just a shift to the right of the Frank-Starling curve, thereby giving increasing efficiency. The fact that the central venous pressure in most of these patients did not rise would suggest to me that this, actually, was not an indication of true failure of the right ventricle.

I think we have looked too long at filling pressures as the measure of resuscitation of our patients who are in shock for any reason. We should instead turn to resuscitation to a relatively normal blood volume, to a relatively normal cardiac output, with normal, or low normal, pulmonary artery pressures and pulmonary artery resistance, particularly, maintaining low pulmonary artery and systemic resistances. In most of the patients, this is going to require the use of some vasodilator, such as nitroprusside, which will vasodilate the peripheral as well as the pulmonary vasculature. We find in most of our patients, and certainly our experimental dogs, that the pulmonary resistance is going to rise two- to four-fold. And I believe that Dr. Greenfield's work here demonstrated that those who were in difficulty were those who had a rise in pulmonary resistance.

So my question would be: Is this really a dysfunction, or is this the normal Frank-Starling response to the increased afterload that is imposed on the right ventricle?

DR. JAMES V. MALONEY, JR. (Los Angeles, California): Dr. Hoffman and Dr. Greenfield and their associates have identified something that I'm sure all of us must have seen, but not recognized. I think these patients have a standard type myocardial infarction that is normally seen on the left side of the heart, by the following mechanism.

The left ventricle, as you recall, during systole normally has a coronary driving pressure of 120 in the aortic root and in the coronary arteries. Therefore, no flow can go to the left ventricular myocardium during systole. During diastole, when the aortic pressure is 80, and end diastolic pressure in the ventricle is 10, all the coronary flow to the left ventricle occurs.

The right ventricle is quite different. During systole, the pressure in the coronary artery is 120, and the pressure in the right ventricle normally is 30; so the right ventricle gets, probably, half its flow during systole, and in addition, it gets the rest of its flow during diastole, when the aortic pressure is 80, and right ventricular pressure, for example, is 5.

However, in shock, quite a different set of circumstances occurs, particularly if one has pulmonary hypertension. The right ventricle cannot get adequate blood supply unless blood is delivered during systole. Any newborn infant who has isolated pulmonary valvular stenosis, who has a Blalock shunt performed—essentially, all of them die, and the reason is that the high pressure persists in the right ventricle, and when you do a shunt, you reduce diastolic pressure, and therefore no coronary flow occurs.

As far as the clinical syndrome goes, when we used to damage hearts for an hour or two during cardiac bypass, some of the patients died immediately, as Dr. Greenfield's patients did, and some, when studied remotely, later, have decreased ejection fraction and high diastolic filling pressures. And it was with increasing excitement as this paper unfolded that I saw that exactly the same thing occurs here. And then the *piece de resistance* was when Dr. Greenfield said that the one correlate they found in this syndrome was that if the pulmonary vascular resistance index is high, it is associated with deterioration. Of course, what that means is that the pulmonary vascular resistance index is high, the pressure on the right side of the heart is high, and therefore the pressure in the aortic route is not high enough during that period of shock to supply the right ventricle with blood. And what we are seeing here, I believe, is right ventricular myocardial infarction in the presence of normal coronary arteries, which is a condition which we have recognized in the cardiac field in the last 4 or 5 years as occurring in the left side of the heart as well.

I am astonished that all of us have seen this syndrome so far in the past and have failed to recognize it. And I suggest this as an alternative explanation.