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Circulatory responses to afterloading with phenylephrine in hyperdynamic sepsis

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We assessed cardiac function by acute pressure loading with phenylephrine in 7 patients who had hyperdynamic sepsis and in 8 patients who had heart disease. All patients with sepsis had a positive Limulus lysate test, a septic focus, and a cardiac output (CO) greater than 6.0 L/min. Phenylephrine was given iv to elevate systolic arterial pressure by 30 mm Hg. Cardiac index (CI) and stroke index (SI) increased significantly in patients with hyperdynamic sepsis, whereas systemic vascular resistance index (SVRI) showed no change. In patients with heart disease, CI and SI decreased significantly, whereas SVRI increased significantly. The marked differences in response to phenylephrine by the two groups suggest lack of cardiac dysfunction in patients with hyperdynamic sepsis.

The question of whether cardiac dysfunction is a physiological determinant of circulatory failure during hyperdynamic sepsis is complicated by indefinite diagnostic criteria for sepsis, differences in the pathophysiological state of the disease, and differences in measures used to assess cardiac function.[1-8]

Increasing resistance to left ventricular ejection by acute pressure-loading with angiotensin or phenylephrine stresses the myocardium, which should reveal latent cardiac dysfunction.[9, 10] The present study describes a marked difference in the response to acute pressure-loading with phenylephrine between patients with hyperdynamic sepsis and those with cardiac disease.

SUBJECTS AND METHODS

This study included 7 hyperdynamic septic patients admitted to the ICU, Osaka University Hospital, between October 1978 and April 1980 (Table 1). None had a previous history of cardiac disease or congestive heart failure before the development of sepsis. The criteria of hyperdynamic sepsis were a positive Limulus lysate test, presence of a septic focus, and CO greater than 6.0 L/min.

Eight patients with cardiac disease, admitted to the ICU during the same period, were used as the control group (Table 1). Six of these patients had ischemic heart disease and 2 had rheumatic heart disease. All patients received appropriate respiratory, circulatory and nutritional care.

Hemodynamic studies were performed before and during phenylephrine administration. CO was determined by the dye dilution method. A central vein and a radial artery were cannulated and the pressures monitored with a pressure transducer. A lead II ECG was continuously monitored. Simultaneous determinations of systolic and diastolic arterial pressures (SAP and DAP), CO, heart rate (HR), and central venous pressure (CVP) were performed when the patient's hemodynamic condition stabilized. Mean arterial pressure (MAP), systemic vascular resistance (SVR), and stroke volume (SV) were calculated by standard formulas. CO, SV, and SVR were indexed per square meter of body surface area.

Phenylephrine (25 mg diluted in 300 ml of 5% fructose in water) was infused over 5–10 min to raise SAP by approximately 30 mm Hg. An infusion rate of approximately 70 μg/min of phenylephrine was required to maintain the SAP at this level throughout the study period.

The hemodynamic values before and during phenylephrine administration were compared using the paired or unpaired t-test.

RESULTS

There was no significant difference in baseline values of SAP, MAP, CVP, and HR between the two groups (Table 2, Fig. 1). Phenylephrine significantly increased SAP, CVP, and calculated MAP in both septic and cardiac groups. HR decreased in both groups, but the change was significant only in the septic group.

Although CI, SI, and SVRI were similar within each group, baseline values varied markedly between groups (Table 2, Fig. 2). In response to phenylephrine, CI and SI increased significantly in the septic group and decreased significantly in the cardiac group. Mean SVRI did not change significantly in the septic group, whereas in the cardiac group, it increased significantly.

Figure 3 represents the relationship between CVP and SI in response to phenylephrine in both groups. In septic group, the myocardial performance curves shifted to the right and upward at almost same slope, whereas in cardiac group, all curves shifted to the right and downward.

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DISCUSSION

There has been much debate on cardiac function in sepsis.[1-8] Calvin et al.[1] reported that cardiac function was augmented in sepsis. Hess et al.[6] found that dogs with arteriovenous shunt recovered from endotoxin shock more easily than those without shunt and suggested the importance of venous return for the recovery from endotoxin shock. Weisel et al.[7] used volume loading to evaluate the cardiac function curve in septic patients, reporting that cardiac function was depressed from the beginning of the disease. Cardiac function also has been assessed by acute pressure-loading using angiotensin in nonseptic patients.[9]

Our results are similar to those of Calvin et al.[1] and Hess et al.;[6] cardiac function was not depressed in hyperdynamic sepsis. We found a marked difference in

TABLE 1. Clinical summary of the patients[a]

Age	Sex	Primary diagnosis	Complication	Organism
Septic Group				
65	M	Carcinoma, esophagus	Mediastinitis	*Enterobacter*
64	M	Carcinoma, rectum	Peritonitis	*K. pneumoniae, Candida*
69	M	Thoracic aneurysm	Mediastinitis	*P. aeruginosa*
73	M	Carcinoma, stomach	Peritonitis	*P. aeruginosa*
72	M	Liver cirrhosis	Pneumonia	*P. aeruginosa, Candida*
45	M	Carcinoma, bladder	Peritonitis	*P. cepacia, Candida*
56	M	Carcinoma, stomach	Peritonitis	*Enterobacter*
Cardiac group				
69	M	Carcinoma, larynx, COPD	CAD, pulmonary edema	
69	M	Carcinoma, stomach	CAD, pulmonary edema	
57	M	Carcinoma, stomach	CAD, pulmonary edema	
74	F	Carcinoma, rectum	CAD, pulmonary edema	
72	M	Carcinoma, esophagus	CAD	
68	M	PSS	Valvular heart disease	
67	M	Carcinoma, stomach	CAD, pulmonary edema	
56	F	Cerebral infarction	Valvular heart disease	

[a] Abbreviations: K = *Klebsiella*, P = *Pseudomonas*, COPD = chronic obstructive pulmonary disease, CAD = coronary artery disease, PSS = progressive systemic sclerosis.

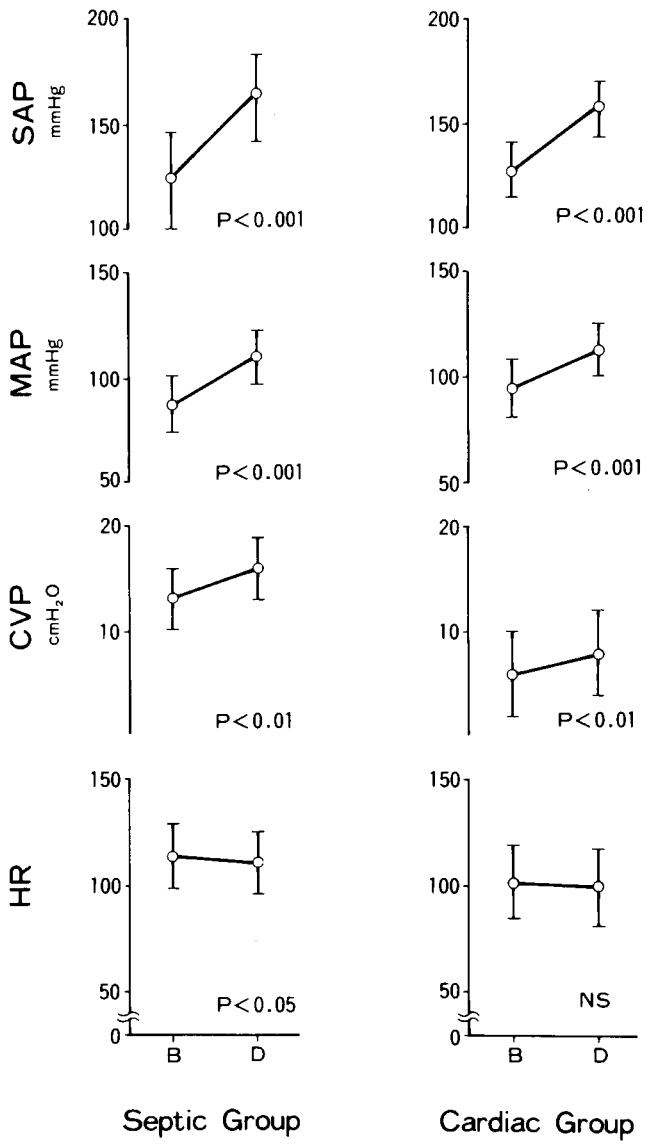

FIG. 1. The changes in SAP, calculated MAP, CVP, and HR before (*B*) and during (*D*) phenylephrine administration. Bars represent 2 SD.

TABLE 2. Changes in hemodynamic values in response to phenylephrine. All values are expressed as mean ± SD; NS = not significant.

	Septic group			Cardiac group		
	Before	During	*P*-value	Before	During	*P*-value
CI (L/min·m²)	5.1 ± 0.9	6.1 ± 1.0	0.001	3.2 ± 0.3	2.8 ± 0.3	0.001
SI (ml/beat·m²)	44 ± 7	55 ± 9	0.001	32 ± 5	28 ± 4	0.001
SVRI (dyne·sec/m⁵·m²)	530 ± 97	576 ± 101	NS	1020 ± 196	1446 ± 247	0.001
SAP (mm Hg)	124 ± 24	162 ± 21	0.001	128 ± 13	156 ± 13	0.001
MAP (mm Hg)	87 ± 14	110 ± 13	0.001	94 ± 14	112 ± 13	0.001
CVP (cm H_2O)	1 ± 3	16 ± 3	0.01	6 ± 4	8 ± 4	0.01
HR (beat/min)	114 ± 16	111 ± 15	0.05	102 ± 17	100 ± 18	NS

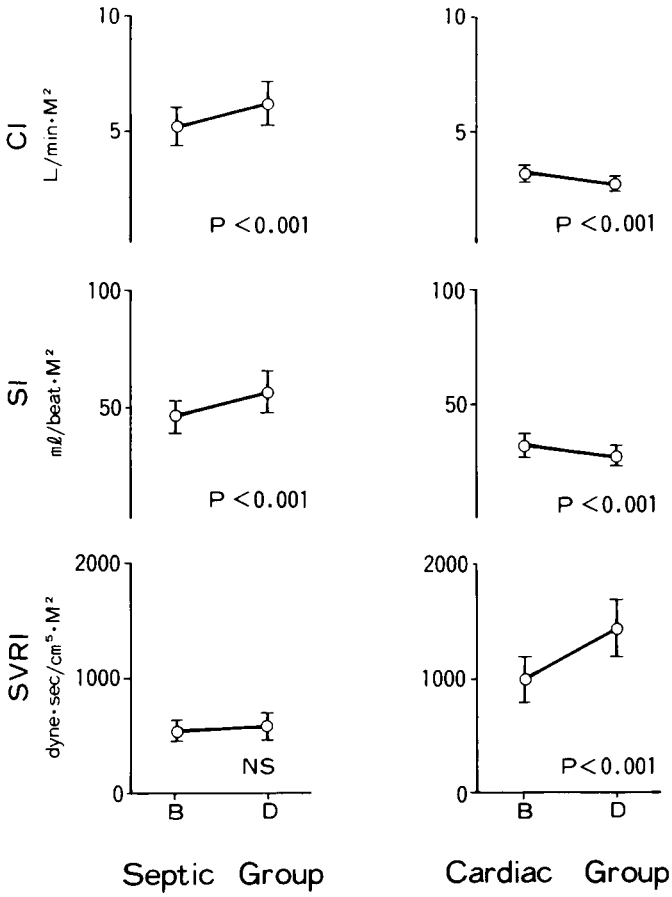

FIG. 2. The changes in CI, SI, and SVRI before (*B*) and during (*D*) phenylephrine administration.

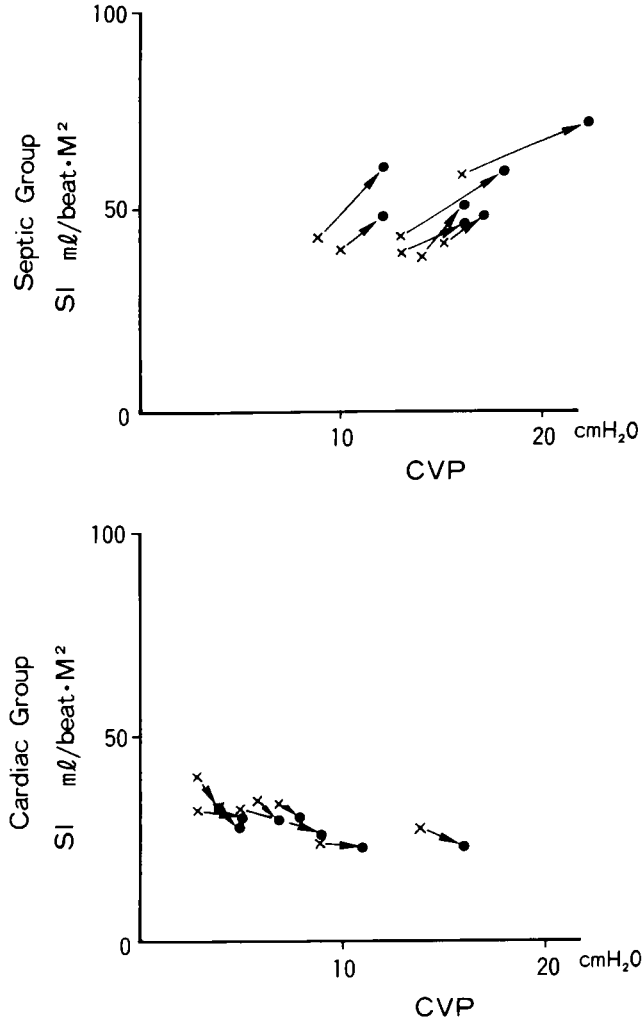

FIG. 3. The relationship between CVP and SI before (*x*) and during (●) phenylephrine administration. *Arrows* indicate the change in response to phenylephrine in each patient.

cardiac response to acute pressure-loading with phenylephrine between septic and cardiac patients. Phenylephrine significantly increased CI and SI in patients with hyperdynamic sepsis, and significantly decreased CI and SI in patients with cardiac disease.

In the normal heart, SV does not change with acute pressure-loading.[11] However, if cardiac function is impaired, acute pressure-loading increases left ventricular end-diastolic pressure (LVEDP) but decreases volume (LVEDV), leading to a decrease in SV. In our cardiac group, decreased SI was consistent with increased cardiac dysfunction, but in the septic group, SI increased significantly.

Figure 4 shows the hypothetical shift in the relationship between the CO and venous return curves[12] before and during acute pressure-loading. Although it seems likely that phenylephrine increased CO by increasing venous return to the heart, it may also act as an inotropic agent in septic patients whose SVR was not significantly changed.

The possible mechanism of the increase in venous return by acute pressure-loading may be explained by the findings of Stockland et al.,[13] who showed that during occlusion of the descending aorta in normal dogs, LVEDV increased significantly. They proposed that in-

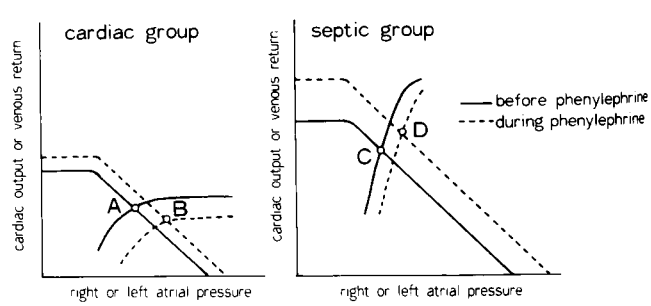

FIG. 4. The hypothetical effect of acute pressure-loading on the CO and venous return curves.

creasing afterload redistributed blood volume from the capacitance vessels to the heart, increasing LVEDV and LVEDP. Weil et al.[14] and others[15, 16] noted pooling of blood in the splanchnic vessels in sepsis. Caldini et al.[17] suggested that the peripheral effect of epinephrine was determined by the change in arterial tone and not by the change in venous tone. In patients with hyperdynamic sepsis, phenylephrine may redistribute blood flow away

from the compartment with the longest time constant (splanchnic area), thereby markedly increasing venous return.

CONCLUSION

Cardiac function during volume loading is usually evaluated by the ventricular function curve. Because it is undesirable to administer a large volume of fluid to patients with cardiac disease or septic lung, other methods should be used. In the present study, we evaluated cardiac function by acute pressure-loading with phenylephrine. Using this technique, it was possible to assess cardiac function in sepsis and septic shock.

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