Pathogenesis of Edema in Constrictive Pericarditis

Studies of Body Water and Sodium, Renal Function, Hemodynamics, and Plasma Hormones Before and After Pericardiectomy

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Background. **The pathogenesis of sodium and water accumulation in chronic constrictive pericarditis is not well understood and may differ from that in patients with chronic congestive heart failure due to myocardial disease. This study was undertaken to investigate some of the mechanisms.**

Methods and Results. **Using standard techniques, the hemodynamics, water and electrolyte spaces, renal function, and plasma concentrations of hormones were measured in 16 patients with untreated constrictive pericarditis and were measured again in eight patients after pericardiectomy. The average hemodynamic measurements were as follows: cardiac output, 1.98 l/min/m^2; right atrial pressure, 22.9 mm Hg; pulmonary wedge pressure, 24.2 mm Hg; and mean pulmonary artery pressure 30.2 mm Hg. The systemic and pulmonary vascular resistances (36.3±2.5 and 3.2±0.3 mm Hg · min · m^2/l, respectively) were increased. Significant increases occurred in total body water (36%), extracellular volume (81%), plasma volume (53%), and exchangeable sodium (63%). The renal plasma flow was only moderately decreased (49%), and the glomerular filtration rate was normal. Significant increases also occurred in plasma concentrations of norepinephrine (3.6 times normal), renin activity (7.2 times normal), aldosterone (3.4 times normal), cortisol (1.4 times normal), growth hormone (21.8 times normal), and atrial natriuretic peptide (5 times normal). The ratio of left atrial to aortic diameter measured by echocardiography was only minimally increased (1.29±0.04), indicating that in constrictive pericarditis the atria are prevented from expanding. The studies repeated after pericardiectomy in the eight patients showed that all measurements returned toward normal.**

Conclusions. **The restricted distensibility of the atria, in constrictive pericarditis, limits the secretion of atrial natriuretic factor and, thus, reduces its natriuretic and diuretic effects. This results in retention of water and sodium greater than that occurring in patients with edema from myocardial disease. The arterial pressure is maintained more by the expansion of the blood volume than by an increase in the peripheral vascular resistance. (*Circulation* 1991;83:1880–1887)**

Chronic constrictive pericarditis is commonly associated with severe retention of sodium and water. Although the pathogenesis of edema in congestive heart failure has been well studied,[1–4] pathogenesis in constrictive pericarditis remains unclear. The mechanisms responsible for the salt and water retention in constrictive pericarditis may differ in

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Preliminary results of this study were presented at the 61st Annual Scientific Sessions of the American Heart Association, November 16, 1988.

Supported by the Indian Council of Medical Research, British Heart Foundation, and EEC contract NST 2J-0071-1-i.

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Received May 9, 1990; revision accepted January 15, 1991.

important respects from those that operate in patients with congestive cardiac failure because the atria in constrictive pericarditis are prevented from expanding, and hence, the stimuli to atrial neuroreceptors and to the release of atrial natriuretic peptide (ANP) are reduced.

We present, here, data on body water and sodium, renal function, hemodynamics, and plasma hormones in a group of 16 patients with constrictive pericarditis and severe sodium and water retention. The patients were not receiving diuretics or other cardiac therapy that may interfere with the hormonal response. Thus, the results may be compared with those that we have reported in patients with untreated congestive cardiac failure due to cardiomyopathy[4] and in normal persons studied with the same techniques. Eight of these patients were restudied after pericardiectomy, also in the absence of any cardiac drug therapy.

Methods

Patients

The studies were performed at the Postgraduate Institute of Medical Education and Research, Chandigarh, India, on 16 consecutive patients with chronic constrictive pericarditis admitted to the hospital. There were 11 males and five females. The age of the patients was 26.1±3.1 years; body surface area was 1.49±0.07 m^2; and the duration of symptoms was 8.6±1.7 months. All patients were short of breath (New York Heart Association functional class, 2.7±0.2). All had mild edema at the ankles, and all except one (R.K.) had ascites. The jugular venous pressure was above the angle of the jaw in all patients, and the liver was enlarged to 5.7±0.5 cm below the right costal margin. The chest radiograph showed a mild increase in cardiothoracic ratio (0.56±0.02). The diagnosis of constrictive pericarditis was made at cardiac catheterization. In all patients, the right atrial, pulmonary artery diastolic, pulmonary artery wedge, and left ventricular end-diastolic pressures were within 5 mm Hg of each other. Constrictive pericarditis was confirmed at surgery in all the patients.

It is our normal practice to withhold any cardiac medication to patients with constrictive pericarditis while they await cardiac surgery. In the present study, none of the patients had received diuretics, digoxin, or any other cardiac therapy for at least 1 month. Because the commonest cause of constrictive pericarditis in our country is believed to be tuberculosis, all patients received antitubercular treatment. Eight patients (indicated with an asterisk in the tables) were restudied at 12.0±1.85 weeks after pericardiectomy. During this period, they received only antitubercular therapy.

Hemodynamics

Hemodynamic measurements were obtained in the postabsorptive state, with a Swan-Ganz thermodilution balloon catheter placed in the pulmonary artery. Arterial pressure was measured with intra-arterial cannulation of the left brachial artery with a 3F Teflon catheter (Seldicath). Pressures were measured with transducers (model 1290C, Hewlett-Packard, Palo Alto, Calif.) and monitor (model 78354A, Hewlett-Packard). The cardiac output was determined by thermodilution (model SP 1445, Gould, Inc., Cleveland, Ohio).[4]

Water and Sodium Spaces and Renal Function

Body water, sodium spaces, and renal function were measured with standard isotope dilution techniques previously described in detail.[4,5] Briefly, plasma volume was calculated from the volume of distribution of 5 μCi iodine-125–labeled human serum albumin 10 minutes after intravenous injection. Extracellular volume and glomerular filtration rate were measured simultaneously with 100 μCi chromium-51–labeled EDTA and calculated by numerical analysis. Effective renal plasma flow was estimated with 100 μCi ^{125}I-labeled sodium iodohippurate and calculated by numerical analysis. Total body water was determined with 100 μCi tritiated water, and total body exchangeable sodium was determined with 20 μCi sodium-22 administered orally. A specially designed protocol allowed all measurements to be made in a single 24-hour period.[4,5]

Plasma Hormones

Plasma hormones were assayed on a 30-ml blood sample drawn from a forearm vein after the patients had been recumbent for 30 minutes. The techniques are described in detail elsewhere.[4,6] Plasma norepinephrine and epinephrine levels were measured by high-performance liquid chromatography with electrochemical detection. Levels of plasma renin activity, aldosterone, vasopressin, cortisol, growth hormone, ANP, and prolactin were measured by radioimmunoassay.

The studies were performed after obtaining written, informed consent from the patients. The study was approved by the ethics committee of the Postgraduate Institute of Medical Education and Research.

Statistical Analysis

The data are presented as mean±SEM. The significance of the difference between various parameters in constrictive pericarditis, control subjects, and congestive heart failure patients was estimated with the Wilcoxon nonparametric test. The effect of pericardiectomy on hemodynamics, body fluid compartment, and hormones was analyzed by the same technique with paired observations.

Results

Effects of Untreated Constrictive Pericarditis

The hemodynamic, water and sodium spaces, renal functions, and the plasma hormone data of the patients with untreated constrictive pericarditis are given in Tables 1, 2, and 3 and in Figure 1. In these

TABLE 1. Hemodynamics in Patients With Untreated Constrictive Pericarditis and in Patients With Edema From Myocardial Disease

Patients	HR (beats/min)	RAP (mm Hg)	PAP (mm Hg)	PAWP (mm Hg)	AoP (mm Hg)	CI (l/min · m²)	PVR (mm Hg · min · m²/l)	SVR (mm Hg · min · m²/l)
Constrictive pericarditis								
B.S.*	93	29	29	23	94	1.9	3.1	33.4
V.I.*	95	24	27	24	82	2.7	1.1	21.4
B.D.	127	24	30	22	86	1.6	5.1	39.8
R.K.*	111	19	29	21	88	2.4	3.4	29.1
K.A.	104	22	28	23	81	2.1	2.4	28.4
A.K.*	122	18	24	20	100	2.4	1.6	33.6
H.A.	...	...	...	...	...	...	...	...
S.U.	110	33	37	27	94	2.3	4.3	26.4
P.A.*	104	20	30	23	90	1.5	4.6	45.7
R.R.	113	29	38	31	100	1.6	4.4	44.6
N.S.*	69	22	29	26	102	1.5	2.0	53.3
B.H.	100	17	26	22	69	2.1	1.9	24.5
R.K.	104	22	30	22	110	2.7	3.0	32.8
T.A.*	90	22	34	28	101	2.0	3.0	39.3
H.Y.	93	19	33	26	86	1.7	4.1	39.6
M.A.*	125	23	29	25	84	1.2	3.5	53.0
Mean	104.0	22.9	30.2	24.2	91.1	1.98	3.2	36.3
SEM	3.9	1.2	1.0	0.8	2.7	0.12	0.3	2.5
n	15	15	15	15	15	15	15	15
Congestive heart failure								
Mean	114.8	15.0	43.7	29.9	99.6	1.75	7.9	47.2
SEM	10.9	2.3	2.7	1.4	5.0	0.11	0.6	1.8
n	8	7	7	7	8	7	7	7
p (vs. CP)	0.2510	0.0026	<0.0001	0.0010	0.1044	0.2540	<0.0001	0.0121

*These patients were also studied after pericardiectomy (see Table 4).
Congestive heart failure data are from Reference 4.
HR, heart rate; RAP, right atrial pressure; PAP, mean pulmonary artery pressure; PAWP, pulmonary artery wedge pressure; AoP, mean aortic pressure; CI, cardiac index; PVR, pulmonary vascular resistance: (PAP−PAWP)/CI; SVR, systemic vascular resistance: (AoP−RAP)/CI; CP, constrictive pericarditis.

tables and Figure 1, our previously published data[4] from normal subjects and from patients with edema associated with severe myocardial disease, obtained using identical methods, are also included.

Hemodynamics. All the patients with constrictive pericarditis had a resting tachycardia. The average cardiac index (1.98±0.12 l/min · m²) was reduced to about half the normal. The pulmonary artery diastolic (24.3±0.8 mm Hg), pulmonary artery wedge (24.2±0.8 mm Hg), and right atrial (22.9±1.2 mm Hg) pressures were all raised and were within 5 mm Hg of each other, confirming the diagnosis of constrictive pericarditis. The pulmonary (3.2±0.3 mm Hg · min · m²/l) and systemic vascular (36.3±2.5 mm Hg · min · m²/l) resistances were moderately increased (Table 1 and Figure 1).

Water and sodium spaces and renal function. The water spaces were all greatly increased. Total body water increased by 36% above normal, and the increase was accommodated almost entirely in the extracellular space; the former increased by 195 ml/kg, the latter by 185 ml/kg. The increase in the extracellular space was divided between the extravascular and intravascular compartment but not in proportion to their normal volumes; the increase in total extravascular volume was much greater, 88% compared with an increase of 53% in the plasma volume. Total body exchangeable sodium increased by 63%. Renal plasma flow was reduced, averaging 49% of normal. Glomerular filtration rate was, however, maintained at a normal level. Serum levels of sodium, potassium, urea, and creatinine were within normal limits (Table 2 and Figure 1).

Plasma hormones. In patients with constrictive pericarditis, there were significant increases in plasma renin activity (7.2 times normal), aldosterone (3.4 times normal), ANP (5 times normal), growth hormone (21.8 times normal), and cortisol (1.4 times normal) (Table 3). It is difficult to interpret the concentration of plasma growth hormone in view of the young age of some of the patients. The plasma concentration of norepinephrine was significantly increased (3.6 times normal), but that of epinephrine was not (Table 3).

Effects of Pericardiectomy

Hemodynamics. The effects of pericardiectomy are listed in Table 4. Pericardiectomy significantly de-

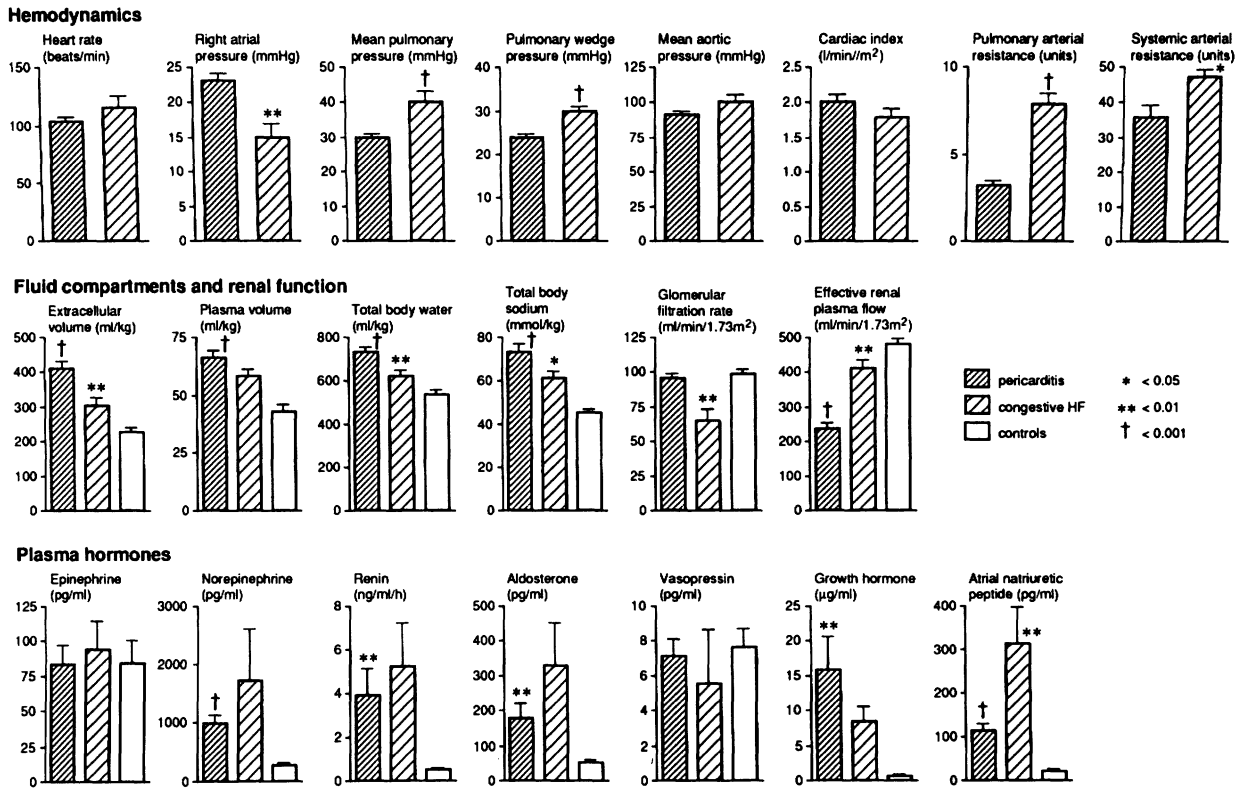

FIGURE 1. *Bar graphs comparing mean±SEM hemodynamic, body compartment, renal function, and plasma hormone data of patients with constrictive pericarditis, untreated congestive heart failure, and normal controls. Significant differences are noted for constrictive pericarditis vs. normal controls, and constrictive pericarditis vs. congestive heart failure. Congestive heart failure and control data are taken from Reference 4.*

creased right atrial pressure, pulmonary arterial pressure, wedge pressure, cardiac index, and systemic vascular resistance to normal levels. Pulmonary vascular resistance decreased, but the decrease was not significant.

Water and sodium spaces and renal function. Pericardiectomy substantially and significantly reduced extracellular volume, plasma volume, total body water, and exchangeable sodium, and it significantly increased renal plasma flow (Table 4). However, none of these measurements had completely reached the normal values shown in Table 2.

Plasma hormones. Pericardiectomy resulted in a return of plasma concentration of norepinephrine to normal. Plasma concentrations of epinephrine, though never increasing above normal limits, also decreased significantly after the operation. Plasma renin activity decreased in all patients except one (N.S.), in whom it did not change at all. Likewise, aldosterone concentration decreased in every patient, but the decrease was not significant. Vasopressin concentration did not change. The mean plasma concentration of ANP decreased substantially, even though the decrease was not significant, and the levels did not entirely return to normal. The maximum effect of pericardiectomy was seen in patients whose levels were high before operation (B.S., N.S., T.A., and M.A.). In three patients with normal levels or only modest elevations of ANP (V.I., A.K., and P.A.), ANP concentration increased slightly and nonsignificantly after the operation. Growth hormone concentrations decreased in five patients, but the decrease was not significant. In one patient (M.A.), it remained unchanged, whereas it increased nonsignificantly in two (N.S., T.A.). Of note, these three patients were adolescents. The normal levels of growth hormone in growing children in our laboratory range from 40 to 50 μg/ml. There was a significant increase in the plasma concentration of prolactin after pericardiectomy, the concentrations of which had been normal before operation. The increase was particularly evident in two young patients (N.S. and T.A.).

Left atrial dimensions. Because the degree of distension of the atria may be an important anatomic distinction between constrictive pericarditis and congestive heart failure due to myocardial disease, we measured the ratio of left atrial to aortic diameter by echocardiography. The ratio was 1.29±0.04 in the patients with constrictive pericarditis and was 1.80±0.14 in the patients with myocardial disease (p=0.0015), which confirms that the left atrium is prevented from expanding in constrictive pericarditis. After surgery, the left atrial to aorta ratio (1.19±0.06) did not change significantly from that before surgery.

TABLE 2. Water Volume, Electrolytes, and Renal Function in Patients With Untreated Constrictive Pericarditis, in Normal Subjects, and in Patients With Edema From Myocardial Disease

Patients	ECV (ml/kg)	PV (ml/kg)	PCV (%)	BV (ml/kg)	TBW (ml/kg)	TBNaE (mmol/kg)	GFR (ml/min/1.73 m^2)	ERPF (ml/min/1.73 m^2)
Constrictive pericarditis								
B.S.*	424	52.9	45	87	677	62	93	206
V.I.*	367	69.1	45	113	622	57	97	274
B.D.	489	72.4	38	107	845	77	109	284
R.K.*	387	61.4	48	105	682	59	126	368
K.A.	337	74.5	45	122	825	69	92	198
A.K.*	398	66.4	51	119	734	75	95	187
H.A.	423	60.5	48	104	860	86	83	143
S.U.	388	54.7	47	92	780	76	84	209
P.A.*	538	61.6	45	101	618	67	69	161
R.R.	...	...	...	...	...	...	...	...
N.S.*	347	66.5	43	106	675	81	109	332
B.H.	433	66.0	45	108	722	85	101	257
R.K.	...	...	...	...	...	...	...	...
T.A.*	326	58.3	49	100	713	63	83	176
H.Y.	499	95.3	53	176	707	60	74	273
M.A.*	...	64.8	60	134	769	103	111	236
Mean	412	66.0	47	112	731	73	95	236
SEM	18	2.8	1.4	5.8	20	3.5	4	17
n	13	14	14	14	14	14	14	14
Normal subjects								
Mean	227	43.2	45.6	61.7	536	44.7	99	479
SEM	13	3.0	1.3	7.0	20	1.9	3	19
n	11	11	7	11	9	10	9	11
p (vs. CP)	<0.0001	<0.0001	0.4516	<0.0001	<0.0001	<0.0001	0.4234	<0.0001
Congestive heart failure								
Mean	301	57.9	39.3	75.1	623	61.3	65	140
SEM	24	2.9	1.6	13	24	3.3	8	25
n	6	6	6	7	7	8	6	6
p (vs. CP)	0.0025	0.104	0.0034	0.0169	0.0047	0.039	0.0022	0.0067

*These patients were also studied after pericardiectomy (see Table 4).
Congestive heart failure and normal data are from Reference 4.
ECV, extracellular volume; PV, plasma volume; PCV, packed cell volume; BV, blood volume; TBW, total body water; TBNaE, total body exchangeable sodium; GFR, glomerular filtration rate; ERPF, effective renal plasma flow; CP, constrictive pericarditis.

Discussion

Untreated Constrictive Pericarditis

In this study, we investigated patients who had classic clinical features and hemodynamic findings of severe chronic constrictive pericarditis.[7,8] These patients had not received any cardiac therapy for at least 1 month before study, and measurements confirmed that the patients had substantial sodium and water retention. On average, they had accumulated 9.6 l of excess water. The renal plasma flow was reduced to approximately half the normal value, but the glomerular filtration rate was preserved. The latter finding is similar to that in less-severe congestive cardiac failure[3] and indicates the presence of an increased glomerular efferent arterial resistance. The hormonal response consisted of a greatly increased activity of the sympathetic nervous system, as judged by the high plasma concentrations of norepinephrine and by stimulation of the renin-angiotensin-aldosterone system. In addition, plasma concentrations of ANP, growth hormone, and cortisol were increased significantly. We are not aware of any similar observations made previously on body water, sodium spaces, renal function, and hormone levels in patients with constrictive pericarditis.

Effects of Pericardiectomy

Pericardiectomy restored all the hemodynamic measurements to normal. The significant increase in cardiac index and the decrease in systemic vascular resistance was accompanied by a substantial and significant increase in the renal plasma flow. Plasma concentration of catecholamines decreased. The average plasma levels of aldosterone and renin activity

TABLE 3. Plasma Hormones in Patients With Untreated Constrictive Pericarditis, in Normal Subjects, and in Patients With Edema From Myocardial Disease

Patients	Epinephrine (pg/ml)	Norepinephrine (pg/ml)	Renin activity (ng/ml/hr)	Aldosterone (pg/ml)	ANP (pg/ml)	Vasopressin (pg/ml)	Growth hormone (μg/ml)	Prolactin (ng/ml)	Cortisol (ng/ml)
Constrictive pericarditis									
B.S.*	166	496	7.6	...	121	...	8.0	5.3	95
V.I.*	...	...	1.9	107	9	5.8	2.3	16.0	110
B.D.	64	877	2.5	223	82	2.1	2.7	3.0	110
R.K.*	66	923	2.7	101	82	7.1	50.0	11.5	69
K.A.	48	524	0.4	31	83	5.8	0.6	5.9	69
A.K.*	123	1,188	0.8	111	46	5.9	7.6	2.0	66
H.A.	79	1,688	9.2	560	89	7.4	29.3	7.1	123
S.U.	...	1,180	2.5	303	128	6.1	16.4	5.1	152
P.A.*	62	1,783	3.1	74	31	16.0	18.1	6.60	100
R.R.	...	...	...	...	...	...	...	...	...
N.S.*	31	652	0.7	89	222	7.9	0.45	17.15	100
B.H.	33	517	5.6	183	193	12.3	41.0	6.00	87
R.K.	...	...	...	...	...	...	...	...	...
T.A.*	98	442	1.0	112	152	5.8	0.5	13.5	98
H.Y.	45	441	1.1	52	126	3.1	3.9	13.1	110
M.A.*	178	2,010	16.0	373	207	7.4	41.0	4.5	103
Mean	82.7	978	3.91	178	112	7.1	15.81	6.20	99.3
SEM	14.2	153	1.17	42	17	1.0	4.67	1.43	6.1
n	12	13	14	13	14	13	14	14	14
Normal subjects									
Mean	83.6	275	0.55	52	22	7.6	0.73	7.30	73.5
SEM	16.4	33	0.05	7	5	1.1	0.16	0.86	8.1
n	15	16	16	16	16	15	16	16	16
p (vs. CP)	0.9666	<0.0001	0.0047	0.0029	<0.0001	0.7496	0.009	0.7102	0.0189
Congestive heart failure									
Mean	93.9	1,719	5.16	330	314	5.5	8.38	16.54	128.8
SEM	19.7	887	2.04	122	84	3.1	2.24	10.21	12.9
n	7	7	8	7	6	7	8	7	8
p (vs. CP)	0.6474	0.2832	0.5734	0.1664	0.0032	0.4586	0.199	0.3076	0.0292

*These patients were also studied after pericardiectomy (see Table 4).
Congestive heart failure and normal subject data are from Reference 4.
ANP, atrial natriuretic peptide; CP, constrictive pericarditis.

also decreased, and although these decreases were not significant, they were substantial in some patients. The transient nature of the renin-angiotensin-aldosterone response,[9] which is subject to feedback control, may explain the great variability. Although the average plasma concentration of ANP decreased substantially, the decrease was not significant, and the levels did not return to normal. The return of neurohormones to normal and of improvement in renal hemodynamics were accompanied by a massive loss of extracellular water and sodium.

Comparison of Findings in Constrictive Pericarditis With Those in Edema From Myocardial Disease

Constrictive pericarditis and congestive heart failure represent two conditions with a similar congestive state. In the former, the underlying myocardium is essentially normal, and the condition is surgically treatable. Our intention was to compare the findings in constrictive pericarditis with those in congestive cardiac failure from myocardial disease. To facilitate this comparison, we included the mean values from our previous study[4] in the tables.

Hemodynamics. The reduction in cardiac index was similar in the two groups. The right atrial pressure was significantly higher in constrictive pericarditis, and the pulmonary arterial pressure and pulmonary wedge pressure were significantly lower. Both the pulmonary and the systemic vascular resistances were significantly lower in the patients with constrictive pericarditis. It is clear, therefore, that the patient with myocardial disease relies to a greater extent on an increase in peripheral resistance to maintain the arterial pressure.

Water, electrolytes, and renal function. There were also notable differences in water and electrolyte spaces and

TABLE 4. Hemodynamics, Water Volume, Electrolytes, Renal Function, and Plasma Hormones in Eight Patients Before and After Pericardiectomy

	Before operation			After operation			
	Mean	SEM	*n*	Mean	SEM	*n*	*p* (paired *t*)
Hemodynamics							
Heart rate (beats/min)	101.1	6.5	8	87.6	5.4	8	0.0838
Right atrial pressure (mm Hg)	22.1	1.2	8	5.3	0.7	8	<0.0001
Mean pulmonary artery pressure (mm Hg)	28.9	1.0	8	18.6	1.6	8	0.0005
Pulmonary wedge pressure (mm Hg)	23.8	0.9	8	11.0	1.2	8	0.0001
Mean aortic pressure (mm Hg)	92.6	2.8	8	90.8	3.4	8	0.5342
Cardiac index (l/min/m^2)	2.0	0.2	8	3.6	0.3	8	0.0035
Pulmonary vascular resistance (mm Hg · min · m^2/l)	2.78	0.4	8	2.3	0.3	8	0.5726
Systemic vascular resistance (mm Hg · min · m^2/l)	38.6	4.0	8	25.9	3.02	8	0.0111
Water volume and renal function							
Extracellular volume (ml/kg)	398	19	7	277	10	7	0.0031
Plasma volume (ml/kg)	62.3	1.4	7	52.2	3.7	7	0.0242
Packed cell volume (%)	48.2	1.4	8	45.1	0.8	8	0.1848
Blood volume (ml/kg)	104.3	2.6	7	86.9	7.3	7	0.0382
Total body water (ml/kg)	674	11	7	552	12	7	0.0020
Total body exchangeable Na (mmol/kg)	66.3	2.3	7	51.4	1.9	7	0.0140
Serum Na (mmol/l)	134.4	1.4	7	138.0	1.1	7	0.2522
Serum K (mmol/l)	4.3	0.1	7	4.4	0.1	7	0.7124
Glomerular filtration rate (l/min/1.73 m^2)	96	5	7	102	9	7	0.2828
Effective renal plasma flow (l/min/1.73 m^2)	243	21	7	382	34	7	0.0026
Serum urea (mg/dl)	34.9	2.2	8	30.4	2.1	8	0.3354
Serum creatinine (mg/dl)	1.53	0.06	8	1.09	0.05	8	0.0142
Hormones							
Epinephrine (pg/ml)	103	21	7	75	22	6	0.017
Norepinephrine (pg/ml)	1,070	166	7	256	15	7	0.0142
Plasma renin activity (ng/ml/hr)	4.21	1.37	8	0.98	0.12	8	0.060
Aldosterone (pg/ml)	138	28	7	38	5	7	0.0580
Atrial natriuretic peptide (pg/ml)	109	21	8	59	10	8	0.1212
Vasopressin (pg/ml)	8.1	1.0	6	7.7	0.5	7	0.6618
Growth hormone (μg/ml)	15.94	5.00	8	7.62	4.86	8	0.2410
Prolactin (ng/ml)	6.59	1.63	8	14.02	2.59	8	0.0169
Cortisol (ng/ml)	92.6	4.2	8	70.9	16.4	8	0.2020

in renal function between the patients with constrictive pericarditis and those with edema from myocardial disease.[4] The renal plasma flow and glomerular filtration rate were significantly higher in the patients with constrictive pericarditis than in those with edema from myocardial disease (by 69% and 46%, respectively). The increases in the plasma volume, extracellular volume, total body water, and exchangeable sodium were also significantly greater in constrictive pericarditis (by 14%, 37%, 17%, and 19%, respectively). These increases in plasma volume and total blood volume must have contributed to the greatly raised venous pressure. Also, the increased renal venous pressure itself possibly acted to increase water and salt retention by the kidney.[10] At the same time, the distensibility of the heart was reduced because of its rigid encasement. This is made apparent by a comparison of the sizes of the hearts. The mean radiographic cardiothoracic ratio was 67.6% in our series of patients with edema from myocardial disease[4] and only 56.4% in the patients with constrictive pericarditis ($p<0.0001$). The heart is a relatively distensible part of the circulatory system and can accommodate a substantial portion of the increased blood volume of patients with edema from myocardial disease. In constrictive pericarditis, this capacity is severely restricted. This might also have contributed to the greatly raised venous and right atrial pressures and, hence, to a greater loss of fluid into the extravascular space and to the significantly greater volume of extravascular water and total body water in patients with constrictive pericarditis. This, however, does not explain why these patients have ascites out of proportion to edema and why, despite markedly raised left atrial pressure, they seldom develop pulmonary edema. Spodick[11] hypothesized a role of low circulating ANP in preventing transcapillary fluid movement in these patients. This needs to be investigated further.

Plasma hormones. Apart from ANP, plasma hormone levels were not significantly different from those in the patients with myocardial disease, although the

average plasma levels of norepinephrine, aldosterone, and renin activity were lower in the patients with constrictive pericarditis. The plasma concentration of ANP was about one third of that in the patients with myocardial disease. A similar moderate rise in the level of ANP was reported in a previous case report.[12] This is consistent with the constrictive process limiting the distension of the atria and, thus, the release of peptide, which is mediated by mechanical stretch.[13]

The lower plasma concentration of ANP in patients with constrictive pericarditis may explain why, despite a higher renal plasma flow and glomerular filtration rate, they had accumulated a significantly greater quantity of total body water and total body exchangeable sodium than did the patients with myocardial disease. In a previous study, we showed that infusion of ANP into patients with untreated edema from myocardial disease had no effect on plasma hormones or hemodynamics but caused significant natriuresis and diuresis.[14] These findings, therefore, suggest that, although the additional vasodilator influence of high circulating plasma concentrations of ANP is not great, their natriuretic and diuretic influence may be more substantial; the greater salt and water retention seen in patients with constrictive pericarditis may be due to the lower levels of circulating ANP found in these patients.

General Conclusions

Constrictive pericarditis imposes a unique impediment on the circulation. The diminished distensibility of the heart specifically reduces the filling of the ventricles and, thereby, cardiac output. It seems likely that the decreased cardiac output tends to decrease the arterial pressure and, thereby, to induce the stimulation of the sympathetic nervous system and the renin-angiotensin-aldosterone system[15,16] in the same way as occurs with myocardial or valvar disease. However, the constrictive process also prevents adequate release of ANP and, thus, may reduce the extent of natriuresis and diuresis due to that hormone. In that way, patients with constrictive pericarditis have a greater expansion of the total body water than do patients with a comparable reduction in cardiac output due to myocardial disease. The arterial blood pressure in constrictive pericarditis is maintained more by an expansion of the blood volume than by an increase in the systemic vascular resistance.

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KEY WORDS • constrictive pericarditis • heart failure • body fluid compartments • blood flow, renal • glomerular filtration rate • plasma hormones

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Circulation. 1991;83:1880-1887
doi: 10.1161/01.CIR.83.6.1880
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7322. Online ISSN: 1524-4539