Hemodynamic Consequences of Severe Pancreatitis

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Fifteen patients with severe pancreatitis underwent cardiovascular monitoring in an intensive care unit. The principal findings were a high cardiac index and a decrease in systemic vascular resistance. A significant negative correlation was found to exist between these two parameters ($p < 0.001$). Severe pancreatitis apparently results in hemodynamic changes similar to those observed in sepsis. The mechanisms responsible for these observations are not known, although circulating vasoactive compounds resulting from pancreatic necrosis remain a strong possibility. Despite demonstrating a significant decrease in left ventricular stroke work index and an abnormal elevation in pulmonary capillary wedge pressure, the existence of a myocardial depressant factor could not be conclusively proved from these data.

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SUSPICION IS MOUNTING that the systemic effects of severe pancreatitis are mediated by circulating substances originating from the inflammed pancreas. Several of these substances have profound effects on the cardiovascular system. The existence of a "myocardial depressant factor" in patients with pancreatitis was demonstrated initially by Lefler et al. in 1971[1]. Recently, Ito et al.[2] have supported this concept by demonstrating a diminution in ventricular performance in patients with pancreatitis. Furthermore, both clinical and experimental studies have shown that pancreatitis results in a marked activation of the kinin system,[3-5] an increase in prostaglandins,[6] and the formation of a substance that increases vascular permeability.[7,8]

In order to characterize further the effects of pancreatitis upon the cardiovascular system, we studied a number of hemodynamic parameters in a group of patients with severe pancreatitis.

Patients and Methods

For the 24-month period 1980–1981, 297 patients with pancreatitis were admitted to the Surgical Service at Grady Memorial Hospital. Thirty-six (12%) of these 297 patients required management in the Surgical Intensive Care Unit. Fifteen of these 36 patients required extensive monitoring of cardiovascular parameters and are the subject of this report.

There were eight men and seven women, with an average age of 51.2 years (range, 31–72). The severity of the underlying pancreatitis present in these patients can be appreciated by the average number of Ranson's prognostic signs (5.2/patient, range 3–8). The pancreatitis in all 15 cases was thought to be due to alcohol. The patients were equitably distributed throughout the Marsielles classification: acute pancreatitis (3), acute relapsing pancreatitis (4), chronic relapsing pancreatitis (5), and chronic pancreatitis (3). Twenty-six major complications were experienced by these 15 patients (Table 1). Fourteen of the 15 required endotracheal intubation and continuous positive airway pressure at some time during their course. Peritoneal dialysis was used in 11 patients, and surgical exploration was carried out in five. Five patients (33%) died, each with five or more of Ranson's prognostic signs.

Central venous pressure catheters to monitor right atrial pressure were inserted, usually by subclavian access. A flow directed pulmonary artery catheter (Swan-Ganz) was placed through the internal jugular or subclavian vein. Pressure lines were connected to Hewlett-Packard transducers (calibrated at the mid chest level with the patient horizontal), whose output was monitored on compatible display instrumentation. All measurements in patients on continuous positive airway pressure were performed during expiration. Cardiac output was determined by the thermistor method using an Edwards thermodilution catheter and slave computer (9520 A). Individual patient values for each parameter represent an average of all values for that parameter during the duration of intensive monitoring.

The following parameters were recorded: heart rate (HR), cardiac output (CO), pulmonary artery pressure (PAP), central venous pressure (CVP), systemic arterial

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TABLE 1. *Measured Parameters*

Patient No.	Complications*	Temp C	Heart Rate (60–90/min)	Cardiac Output (4–8 L/min)	Central Venous Pressure (5–15 cmH_2O)	Pulmonary Capillary Wedge Pressure (4–13 mmHG)	Course†
1	ARDS	37.6	110	6.5	14	22	L
2	ARDS, ARF	37.5	110	6.4	13	16	L
3	Abscess	38.5	120	9.7	12	24	L
4	ARDS	38.0	110	7.9	12	17	L
5	ARDS	37.5	120	7.8	14	16	L
6	ARF	37.4	105	7.8	15	24	D
7	Hemorrhage	36.0	110	3.1	17	19	D
8	ARDS, ARF, C	37.0	120	8.4	20	20	D
9	ARDS	37.5	110	9.4	14	15	L
10	ARDS, ARF, C	37.0	110	8.8	12	18	L
11	ARDS, C, Ascites, Hemorrhage	37.8	110	6.3	26	31	D
12	Abscess	38.6	130	8.2	9	12	L
13	ARDS, C, Hemorrhage	37.0	110	4.4	26	22	L
14	Ascites, C	36.0	90	5.0	7	11	D
15	ARDS	37.0	110	5.6	12	13	L
Mean			112	7.0	14.9	18.6	
SEM			2.3	0.5	1.6	1.4	

* ARDS = Acute respiratory distress syndrome; ARF = Acute renal failure; C = coagulopathy.

† L = living; D = dead.

pressure (SAP), and pulmonary capillary wedge pressure (PCW). From these data, the following values were computed according to the formulas contained in the Appendix: left ventricular stroke volume (LVSV), left ventricular stroke index (LVSI), cardiac index (CI), mean pulmonary artery pressure (MPAP), systemic vascular resistance (SVR), pulmonary vascular resistance (PVR), and left ventricular stroke work index (LVSWI).

Analysis of these data for possible significant correlation between any pair of measured or derived parameters was carried out by linear regression analysis, and significance tested with a t-test.

Results

Measured Parameters

In general, these patients exhibited a marked tachycardia (112 ± 2.3) in the face of a high normal CVP (14.9 ± 1.6 cmH_2O) and an elevated PCW (18.6 ± 1.4 mmHg) (Table 1). The CO was within the high normal range, although only three of the 15 patients (patients 3, 4, and 12) were proved to be septic.

Derived Parameters

The LVSI (33.9 ± 1.9 cc/M^2), the LVSWI (43.3 ± 3.5 $gm\text{-}m/M^2$), and the SVR (964 ± 84 $dyne\text{-}sec\text{-}cm^{-5}$) were abnormally low (Table 2). MPAP (27 ± 1.2 mmHg) was abnormally high. The CI was high normal but would have been abnormally elevated if the two patients with hemorrhage (patients 7 and 13) had been excluded.

Correlations

In this group of patients, the abnormally low systemic vascular resistance was found to be negatively correlated with cardiac index in a highly significant manner ($R = -0.81$; $p < 0.001$) (Fig. 1). This finding was corroborated by a correlation between cardiac output and systemic vascular resistance ($R = -0.80$; $p < 0.001$). In only four other pairings of the hemodynamic parameters were significant linear relationships observed: (1) PCW *vs.* CVP, $R = 0.76$, $p < 0.01$; (2) PCW *vs.* MPAP, $R = 0.74$, $p < 0.01$; (3) CO *vs.* PVR, $R = -0.66$, $p < 0.01$; and (4) CI *vs.* PVR, $R = -0.65$, $p < 0.01$.

Discussion

Pancreatitis is a disease of protean manifestations. In its more severe forms, involvement of any of the organ systems of the body is possible. Indeed, it is the widespread nature of such organ involvement that has lead many to suspect that severe pancreatitis is a systemic disease.

The effects of pancreatitis on the cardiovascular system have received comparatively little attention. Although many workers have demonstrated the presence of various vasoactive compounds in both experimental[3,5–8] and clinical pancreatitis,[1,4] the importance of cardiovascular factors in the pathogenesis of pancreatitis and its complications remains problematic. Because few hemodynamic measurements have ever been made in such patients, it has been impossible to determine whether the cardiovascular changes frequently observed

TABLE 2. *Derived Hemodynamic Parameters**

Patient No.	LVSV† 60–130 cc	LVSI 35–70 cc/M²	CI 2.5–4.0 L/min/M²	MPAP 10–20 mmHG	SVR 1000–1600 dyne-sec/cm⁻⁵	PVR 50–160 dyne-sec/cm⁻⁵	LVSWI 45–60 gm-m/M²
1	70	36.5	3.39	31	1200	134	50.1
2	62	33.0	3.40	27	884	103	39.9
3	60	29.7	4.80	22	768	110	46.9
4	72	41.9	4.59	22	856	55	55.8
5	57	34.3	4.69	30	760	140	41.1
6	74	44.6	4.69	32	588	86	41.2
7	29	17.5	1.87	32	1620	230	16.2
8	71	37.0	4.38	26	560	70	47.3
9	80	42.6	5.00	20	640	80	55.0
10	89	45.4	4.49	25	880	85	76.0
11	57	32.0	3.54	40	1064	215	43.6
12	61	28.8	3.87	18	816	84	36.0
13	40	25.6	2.82	33	1600	240	35.6
14	55	33.1	3.01	20	1210	48	38.3
15	51	27.1	2.98	27	1016	205	27.0
Mean	61.9	33.9	3.83	27	964	126	43.3
SEM	3.9	1.9	0.24	1.6	84	17	3.5

* See appendix for specific formulas.

† LVSV = left ventricular stroke volume; LVSI = left ventricular stroke index; CI = cardiac index; MPAP = mean pulmonary artery pressure; SVR = systemic vascular resistance; PVR = pulmonary vascular resistance; and LVSWI = left ventricular stroke work index.

in patients with pancreatitis are due to circulating vasoactive compounds, or to other mechanisms.

Only two previous studies have dealt with hemodynamic changes in pancreatitis. Ito et al.[2] found an elevated cardiac index (3.51 ± 1.32 L/min/M²), and a decrease in the left ventricular stroke work index (39.5 ± 18.9 gm-m/M²). These observations closely approximate the respective values found in this study. DiCarlo et al.[9] reported similar observations in a group of 21 patients with pancreatitis, but noted that in addition to an increased cardiac index and myocardial depression, there was a marked decrease in total peripheral resistance. This latter observation has been corroborated by the data from the current report.

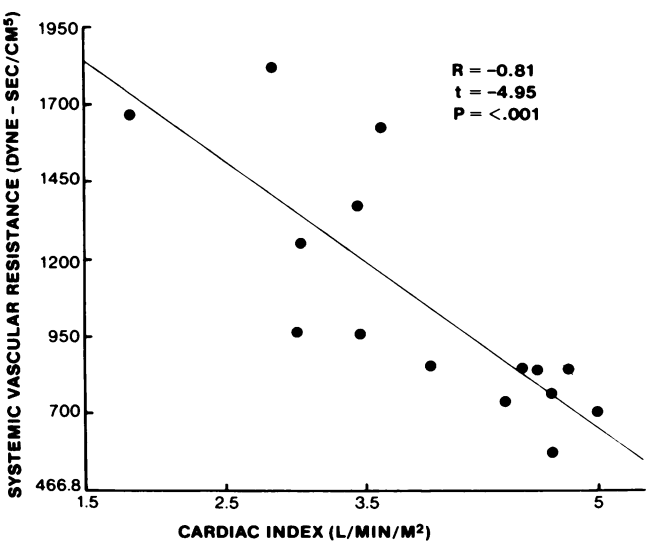

FIG. 1. The highly significant correlation between cardiac index and systemic vascular resistance suggests a dependent relationship.

In effect, patients with severe pancreatitis apparently have a high output, low resistance picture resembling the hemodynamic pattern seen in sepsis.[10,11] Since only three of our 15 patients exhibited any signs of sepsis, other explanations for these observations in this group of patients must be sought. The reason for the observed decrease in systemic vascular resistance and elevation of cardiac index has not been determined specifically by the data in this study. Possible explanations include the opening of arteriovenous shunts, metabolic abnormalities resulting in loss of vascular reactivity, and/or the elaboration of vasodilator compounds by pancreatic inflammation.

The shift in cardiac index toward the upper limit of normal apparently occurs as a result of an increased heart rate and diminished peripheral resistance and occurs despite a decrease in stroke index. Since 14 of these patients were on continuous positive airway pressure, a known depressant of cardiac index,[12] the finding of a high normal cardiac index in this group of patients is even more significant.

There are other findings of interest in this study, although their interpretation is less clear. Pulmonary capillary wedge pressures were abnormally elevated. Because PCW is commonly thought to represent left atrial pressure (left ventricular pre-load), many investigators have used PCW as a measurement of left ventricular function.[13] In this regard, an increase in PCW could be considered consistent with diminished left ventricular

performance when combined with the finding of an abnormally low left ventricular stroke work index (Starling-Frank relationship). However, it must be remembered that pressure measurements were made in patients receiving continuous positive airway pressure, which is known to distort intrathoracic pressure determination. Furthermore, since neither pulmonary nor thoracic compliance was measured in these patients, strict interpretation of the PCW values is not possible. Accordingly, in the absence of pressures corrected for disease-induced changes in compliance, previous studies which estimated left ventricular performance by plotting central venous pressure *vs.* left ventricular stroke work index,[9] or which compared pulmonary capillary wedge pressure with left ventricular stroke work[2] are subject to question.

Further investigation of the hemodynamic changes induced by pancreatitis seems warranted. A more carefully controlled prospective study using more sensitive and sophisticated methodology has been planned.

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Appendix

Methods of Calculation

(1) $LVSV = \frac{CO}{HR}$

LVSV = left ventricular stroke volume
HR = heart rate

(2) $LVSI = \frac{LVSV}{BSA}$

LVSI = left ventricular stroke index (ml/beat/M^2)

(3) $CI = \frac{CO}{BSA}$

CI = cardiac index (L/min/M^2)
CO = cardiac output (L/min)
BSA = body surface area (M^2)

(4) $SVR = \frac{\overline{SAP} - \overline{RAP}}{CO}$

SVR = systemic vascular resistance (hybrid units)

$\overline{SAP}$ = mean systemic arterial pressure (mmHG)

$\overline{RAP}$ = mean right atrial pressure (mmHG)

(5) $PVR = \frac{\overline{MPA} - \overline{PCW}}{CO}$

PVR = pulmonary vascular resistance (hybrid units)

$\overline{PCW}$ = mean pulmonary wedge pressure (mmHG)

(6) $LVSWI = LVSI \times \overline{SAP}$

LVSWI = left ventricular stroke work index (gm-meters/M^2)