Effects of Portal Vein Occlusion on Myocardial Contractility

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We studied canine left ventricular contractile performance following 15 min of portal vein occlusion by analyzing the end-systolic pressure diameter relationship (ESPDR) which many investigators have reported as being independent of changes in preload and afterload but sensitive to changes in ventricular contractility. Portal vein occlusion for 15 min decreased the mean arterial pressure, left ventricular peak systolic pressure, and cardiac index, while the release of the occlusion gradually increased these values, although it did not restore them to the control values. The systemic vascular resistance index increased during portal vein occlusion and returned to the control values after release. Left ventricular end diastolic diameter decreased during portal clamping and returned to the control values after release. ESPDR and percent shortening were not significantly changed during or after portal clamping. These rersults indicate that the decrease in blood pressure during portal vein occlusion was not due to a reduction in myocardial contractility but rather was due to a reduction in preload. (Key words: portal vein occlusion, myocardial contractility, end-systolic pressure diameter relationship)

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Occlusion of the portal vein may be performed during liver resection[1] or management of extensive liver injury[2] to decrease bleeding. It is well known that in many species, portal clamping for more than 30 min leads to circulatory collapse[3,4]. We reported that a marked reduction of blood pressure and cardiac output followed portal vein occlusion in dogs during halothane anesthesia[5] and suggested that the cause of this might be a reduction of preload, a decrease in cardiac contractility due to release of some humoral factor, or a combination of both these effects. Therefore, the purpose of this study was to determine whether myocardial contractility was depressed by portal vein occlusion in dogs during pentobarbital anesthesia. The study was divided into two parts. First, we determined the hemodynamic characteristics during and after portal vein occlusion. Second, we assessed the left ventricular inotropic state by measuring the slope of the end-systolic pressure diameter relationship (ESPDR). Other investigators have reported that ESPDR is independent of preload and afterload and relatively insensitive to an altered heart rate. However, ESPDR is sensitive to changes in contractility[6,7], and therefore can be used to

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assess changes in cardiac contractility.

Materials and Methods

The studies were conducted under the guidelines of the Animal Care Committee of the University of Chiba School of Medicine. Sixteen adult mongrel dogs (11–31 kg) were anesthetized with pentobarbital 30 $mg \cdot kg^{-1}$ intravenously, and intubated. Anesthesia was maintained with a continuous infusion of pentobarbital at 1 $mg \cdot kg^{-1} \cdot hr^{-1}$. Each animal was mechanically ventilated with 100% oxygen and the tidal volume was adjusted to maintain the Pa_{CO_2} between 35 and 45 mmHg. Each dog received lactated Ringer's solution 4 $ml \cdot kg^{-1} \cdot hr^{-1}$ throughout the experimental period. Two separate experiments were then performed.

Experiment 1: Five dogs were studied. A femoral artery was cannulated and arterial pressure measured. A femoral vein was also cannulated and a Swan-Ganz catheter was advanced into the pulmonary artery and the position verified by the characteristic pressure trace. The Swan-Ganz catheter was used to determine cardiac output using the thermodilution method. Pulmonary artery pressure (PAP) and pulmonary capillary wedge pressure (PCWP) were also measured. A jugular vein was cannulated for central venous pressure measurement and for injection of cold saline. Cardiac index (CI), systemic vascular resistance (SVR) and pulmonary vascular resistance (PVR) were calculated using the standard formulae. After initial preparations were completed a midline celiotomy was performed and the portal vein was isolated.

Following surgical preparation, each dog was allowed to stabilize for about 60 min, then the control cardiovascular data were obtained. The portal vein was clamped for 15 min. At 5, 10 and 15 min during the period of portal occlusion, complete sets of the hemodynamic data were repeated. Following 15 min of occlusion, the clamp was released and perfusion restored. After reperfusion, the hemodynamic measurements were obtained at 5, 10, 15, 30 min following release of the occlusion, then every 30 min until 120 min postrelease.

Experiment 2: Eleven dogs were studied. A fluid-filled catheter was passed from a femoral artery to an aortic arch and arterial pressure was measured. A left thoracotomy was then performed at the sixth intercostal space and a pair of ultrasonic crystals, for determination of left ventricular anterior-posterior short axis internal diameter, were implanted on the endocardial surface on opposite sides of the left ventricle, approximately one-third of the distance from the apex to the base[8]. An oscilloscope was used to ensure proper alignment of the crystals. A catheter-tip micromanometer was placed through the left ventricular apex and secured with a purse-string suture and A balloon tipped aortic occlusion catheter was positioned in a descending aorta through the other femoral artery. The chest was then closed.

A midline celiotomy was then performed and the portal vein was isolated. After these surgical preparations, each dog was allowed to stabilize for about 60 min. Analogue recordings were made on an 6-channel, forced ink oscillograph. The following measurements were obtained: left ventricular pressure (LVP), first derivative of LVP with respect to time (dP/dt), left ventricular short axis diameter (LVD), heart rate, arterial pressure, and LVP/LVD. Figure 1 shows an actual recording obtained from one dog. The end diastolic point was defined by the R-wave of the ECG. The end systolic point was defined at the point of maximal LVP/LVD[9–11]. This criterion is in accordance with the definition that end-systole is the instant at which the contractile process reaches its maximum[12–14]. We measured left ventricular end diastolic pressure (LVEDP), left ventricular end systolic pressure (LVESP), left ventricular end diastolic diameter (LVEDD), and left ventricular end systolic diameter (LVESD), and the %shortening was calculated. ESPDR was calculated from data obtained duringa transient 10 sec aortic occlusion[15]. As afterload progressively increased during successive heart beats, a wide range of values for LVESP and LVESD

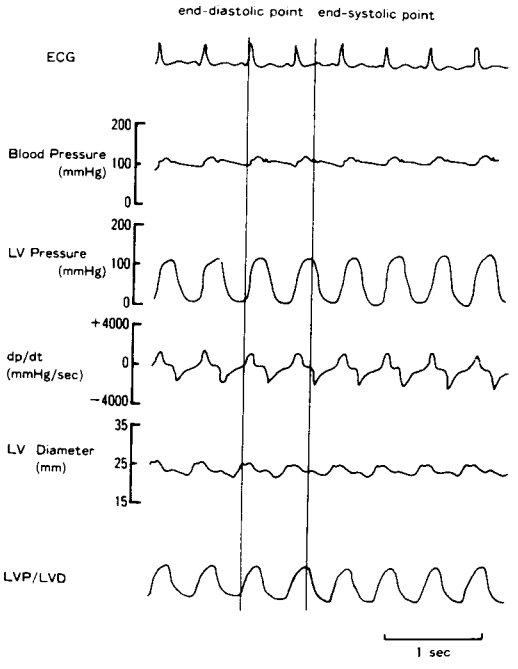

Fig. 1. Figure 1 shows an actual recording obtained from one dog.

The end diastolic point was defined by the R-wave of ECG. End systolic point was defined as the point of maximal left ventricular pressure/left ventricular diameter (LVP/LVD).

was obtained. Linear regression was performed on these data pairs to determine the slope and intercept values. Regression analysis of variance was performed to determine the statistical significance of the observed data and any r^2 value being < 0.8 was discarded.

After control data were obtained, the portal vein was clamped for 15 min in 6 dogs. In the other 5 control dogs the portal vein was not clamped. The cardiovascular measurements were repeated at 5, 10 and 15 min during and after portal clamping, then every 30 min to 120 min postrelease.

These data were analyzed by two-way analysis of variance for repeated measures. When an overall difference was found, individual comparisons were made using the paired t test with the Bonferroni correction for multiple simultaneous comparisons. Values are reported as mean ± SEM.

Results

Experiment 1: Table 1 presents the data from experiment 1. Heart rate increased following 5 min of portal vein occlusion but was not significantly changed at any other time during potal vein occlusion or follow-

Table 1. Hemodynamic date in experiment 1

	control	portal vein occlusion			after release						
		5min	10min	15min	5min	10min	15min	30min	60min	90min	120min
HR	160	183*	157	153	146	150	153	159	164	165	166
(beats·min^{-1})	15	15	8	10	11	12	12	14	15	13	14
MAP	136	80*	59*	51*	93*	96*	99*	107*	111*	111*	114*
(mmHg)	11	6	10	6	6	6	5	6	5	7	6
MPAP	12.8	5.8*	5.5*	5.4*	11.4	11.1	11.6	11.8	13.0	13.5	13.9
(mmHg)	4.1	2.2	2.3	2.4	3.8	3.8	3.9	4.9	5.1	5.5	5.4
PCWP	8.2	1.8	2.6	1.6	4.1	4.2	5.3	7.9	7.4	9.1	8.4
(mmHg)	4.6	1.6	1.6	1.5	2.5	2.5	3.3	4.9	5.2	5.0	5.0
CI	2.9	1.0*	0.9*	0.9*	1.8*	1.9*	2.0*	2.3*	2.4*	2.3*	2.4*
(l·min^{-1}·m^{-2})	0.3	0.1	0.1	0.1	0.4	0.4	0.3	0.4	0.4	0.4	0.5
SVR	3894	6906*	5311*	4731	4447	4359	4174	4062	4123	4147	4326
(dynes sec·cm^{-5})	451	858	941	678	613	559	441	581	671	563	747
PVR	170	333	320	352	312	271	274	237	283	239	279
(dynes sec·cm^{-5})	66	80	115	78	33	30	43	14	16	28	17

Values are mean ± SEM; n = 5 dogs; *:$P < 0.05$ compared with the control

Table 2. Left ventricular pressure and dimension data in control group of experiment 2

	control	15 min	30 min	45 min	75 min	105 min	135 min
LVSP	143	147	148	146	154	149	156
(mmHg)	7	3	5	8	9	15	17
LVEDP	3.0	4.0	2.3	2.7	2.7	3.5	2.8
(mmHg)	1.2	1.2	0.2	0.5	0.8	0.9	1.1
LVEDD	28.9	28.7	28.9	28.8	28.7	28.3	28.4
(mm)	5.7	5.7	5.7	5.9	5.9	5.7	5.5
%shortening	14.0	14.0	13.7	14.9	14.4	14.6	14.4
(%)	2.8	3.4	3.8	3.7	3.9	3.1	3.4
%Changes of slope	100	103.2	108.1	105.5	100.0	116.0	114.3
(%)	0	8.3	20.0	11.6	14.3	21.2	10.9
D_0	23.5	23.3	23.6	23.5	23.2	23.7	23.4
(mm)	5.0	4.7	4.4	4.7	4.6	4.3	4.7

Values are mean ± SE; n = 5 dogs; LVSP, left ventricular peak systolic pressure; LVEDP, left ventricular end-diastolic pressure; LVEDD, left ventricular end-diastolic diameter; %Shortening, (LVEDD-left ventricular end-systolic diameter)/LVEDD*100; %Changes of slope, %Changes of slope of ESPDR (%control); D_0, diameter intercept of the ESPDR slope line.

Table 3. Left ventricular pressure and dimension data in portal clamp group of experiment 2

	control	portal vein occlusion			after release					
		5min	10min	15min	5min	10min	15min	30min	60min	90min	120min
LVSP	141	96*	96*	94*	128	131	130	135	140	140	139
(mmHg)	11	14	15	16	16	12	13	13	14	14	15
LVEDP	5.2	4.0	2.6	2.3	6.0	5.2	4.5	4.3	5.3	6.2	6.4
(mmHg)	1.9	2.8	2.1	2.3	1.7	1.8	1.9	1.6	1.7	2.4	2.2
LVEDD	37.4	35.1*	35.0*	34.8*	37.9	37.3	37.1	36.9	37.0	37.5	37.6
(mm)	7.0	6.7	6.9	6.5	7.5	7.1	7.0	6.8	6.8	7.3	7.2
%shortening	10.8	10.2	10.3	11.0	10.2	12.7	10.8	10.9	10.8	10.2	10.6
(%)	2.2	2.0	2.1	2.4	2.5	2.9	2.7	2.3	2.2	2.5	2.4
%Changes of slope	100	106.0	113.3	119.0	115.1	109.7	107.7	148.0	144.2	153.2	118.3
(%)	0	10.9	16.7	16.6	24.7	18.0	20.4	28.6	16.7	30.9	9.6
D_0	30.2	31.5	31.6	31.5	31.6	31.2	30.4	31.0	32.0	32.4	31.9
(mm)	5.2	5.0	4.7	4.8	5.3	4.8	5.9	5.7	5.6	5.8	5.1

Values are mean ± SEM; n = 6 dogs; LVSP, left ventricular peak systolic pressure; LVEDP, left ventricular end-diastolic pressure; LVEDD, left ventricular end-diastolic diameter; %Shortening, (LVEDD-left ventricular end-systolic diameter)/LVEDD*100; %Changes of slope, %Changes of slope of ESPDR (%control); D_0, diameter intercept of the ESPDR slope line; *:$P < 0.05$ compared with the control.

ing release. Mean arterial pressure (MAP) decreased markedly during occlusion and increased gradually after release. However, even at 120 min following release it had not returned to the control value. Mean pulmonary artery pressure (MPAP) decreased significantly during clamping and returned to the control value after release. The changes in PCWP showed great individual variations but the changes were not statistically significant. However, there was a tendency for PCWP to decrease during clamping and to return toward control value after release. CI decreased markedly during clamping and al-

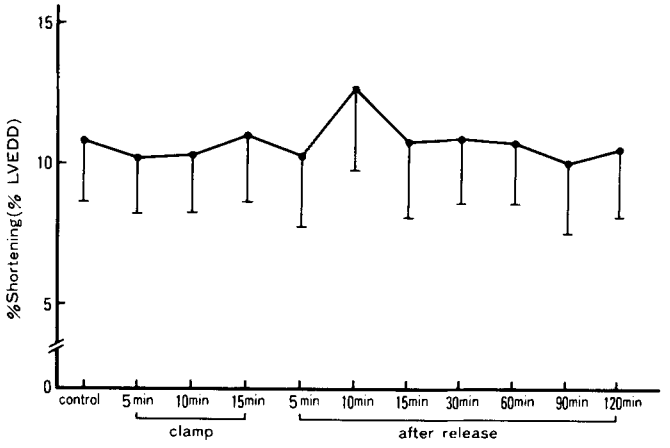

Fig. 2. The effects of portal vein occlusionon percent shortening.

Data presented are mean ± SEM. The changes were not significant.

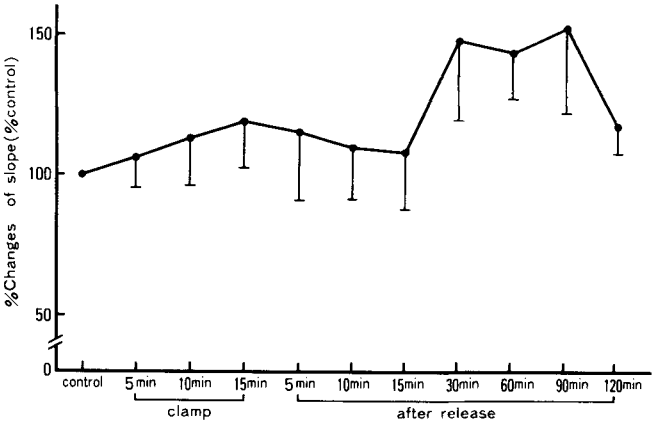

Fig. 3. The effects of portal vein occlusion on %changes of slope of ESPDR.

Data presented are mean ± SEM. Although slope of ESPDR tends to increase at 30 min after release and remains high thereafter, there are no significant changes.

though it increased after release, it did not return to the control value. SVR increased significantly at 5 and 10 min during occlusion and returned to the control value after release. PVR was not significantly changed during or following portal occlusion. These hemodynamic changes during portal vein occlusion are similar to the results which we previously reported[5].

Experiment 2: Table 2 presents the hemodynamic variables of the control group of dogs that did not have the portal vein clamped. There was no significant change in any variables throughout the study period in these animals.

Table 3 and figures 2 and 3 present the data from the dogs that had the portal vein occluded. Left ventricular systolic pressure (LVSP) significantly decreased during portal vein occlusion and gradually increased, returning to the control value, after release. There was no significant change in LVEDP during or after portal vein occlusion. LVEDD decreased significantly during clamping and returned to control after release. This suggests that preload is decreased during portal vein occlusion. There was no significant change in %shortening (fig. 2) suggesting that the ejection fraction did not change during and after portal vein occlusion. Figure 3 shows %change of the slope of ESPDR. Although ESPDR tended to increase at 30 min after release, there was no significant change in the slope during or after portal vein occlusion nor did intercept values change significantly.

Discussion

It is well known that an acute occlusion of the portal vein results in rapid cardiovascular collapse in many species. The cause of the collapse has been ascribed to a reduction of preload due to massive pooling of blood in the splanchnic bed[16] or a decrease in cardiac contractility due to metabolic acidosis[17] or the release of humoral factors from ischemic gut[18,19]. However, measurements of the direct inotropic effects produced by portal vein occlusion have been hampered because of difficulty in assessing changes in contractility, independent of concurrent changes in loading conditions. Mahler[6] and Goldfarb[20] have previously reported that the slope of ESPDR is independent of preload and afterload but is sensitive to changes in the contractile state of the ventricle. In this study we examined the hypothesis that acute portal vein occlusion followed by reperfusion would produce marked depression in cardiac contractility by measuring the slope of the ESPDR.

MAP and LVSP decreased markedly during portal vein occlusion and tended to rise after release of the occlusion but were not restored to control values. CI also changed in the same pattern as MAP. Other authors have reported the similar hemodynamic changes in dogs during and after occlusion of the portal vein[5,19,21]. SVRI increased during portal vein occlusion and tended to decrease and returned to the control value after release. These results support the concept that the decrease in cardiac output, rather than peripheral vascular collapse, initiates depression of MAP and LVSP.

Although slope of ESPDR tended to increase at 30 min after release of portal vein occlusion and remained high thereafter, there were no significant change in the slope or the value of X intercept of ESPDR at any time during the experiment. In addition, the percent shortening, another index of cardiac inotropic state, also showed no significant change. This suggests that the cardiac inotropic state was not depressed by 15 min of portal vein occlusion during pentobarbital anesthesia.

Many authors have reported that prolonged splanchnic congestion and subsequent reperfusion in dogs results in depression of cardiac contractility and peripheral vascular collapse due to release of acid metabolites[19] and neuropeptides (e.g., vasoactive intestinal polypeptide, met-enkephalin) from clamped vascular beds[22]. However, a marked decrease in MAP and CI may activate reflexes through cardiopulmonary baroreceptors[23] and Andrews et al. reported that an increase in portal venous pressure activated pressoreceptors in the portal venous system, increasing systemic arterial pressure[24]. Moreover, Gaumann et al. reported that ischemia of gut and subsequent intestinal reperfusion increases adrenal secretion of catecholamines[22]. This may increase heart rate, peripheral vascular resistance, and cardiac contractility. We suppose that myocardial contractility and systemic vascular resistance remained at or above the preclamping level during 15 min of portal vein occlusion because these pressor effects counteract the depressor effects due to release of acid metabolites and neuropeptides.

Although PCWP and LVEDP did not change significantly, LVEDD decreased during portal vein occlusion. Vanhoutte et al. reported that only a 1 mmHg change in LAP caused a 12 $ml \cdot kg^{-1} \cdot min^{-1}$ change in cardiac output on the average[25]. We assume, therefore, that we could not detect the changes in PCWP and LVEDP because of the small changes in pressure. This results show that marked decrease in CI during portal clamping results from reduction of preload. We assume that the decrease in preload results from massive pooling of blood in the splanchnic bed because of the lack of portosystemic anastomosis in dogs[16,19,26]. After release of occlusion, MAP and CI did not return to the preclamping level. Yamamoto et al. reported that splanchnic congestion during portal vein occlusion resulted in intestinal sequestration of plasma and could cause a decrease in circulatory blood volume after release[14]. We suppose that the intestinal sequestration of plasma may contribute to the decrease in MAP and CI after release,

when compared to the control values.

In conclusion, in this study, portal vein occlusion for 15 min markedly decreased LVSP and CI and release of the clamp resulted in an increase in these values, although it did not restore them to the control values. SVR increased during portal vein occlusion and returned to the control value after release. LVEDD decreased during portal vein occlusion. Percent shortening, ESPDR were not significantly changed during and after portal vein occlusion. These results suggest that the marked decrease in blood pressure during portal vein occlusion was due primarily to a reduction in preload with no significant effect upon myocardial contractility.

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