Active Changes In Tone in the Canine Vena Cava

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ABSTRACT
Active changes in tone of the superior vena cava were studied in dogs several days after recovery from surgery. The diameter was measured continuously by sonar technique and distending pressure by Silastic cannulas. An occlusion cuff at the junction of the superior vena cava and atrium generated a passive range of pressure-radius data in the control state. Interventions included catecholamine infusion, fright, and exercise. In most instances, active constriction with norepinephrine could be shown by a pressure-radius curve that was steeper and displaced toward the pressure axis. The constricted curves were frequently, but not invariably, sigmoid, whereas control occlusion curves were arcuate. Isoproterenol also produced active constriction of the superior vena cava, as did fright and moderate exercise.

KEY WORDS exercise capacitance vessels venoconstriction isoproterenol sonar dimension transducer norepinephrine fright

...That the venous capacity is controlled is generally accepted, but the extent and mechanisms of this control are largely unknown. The vena cava is immediately adjacent to the heart, and variations in tone could produce prompt changes in cardiac output by altering the filling pressure for the right ventricle and the back pressure for the systemic circulation. In 1966 we reported our studies of pressure, flow, and diameter of the superior vena cava in intact dogs (1), but our conclusions were limited by a nonquantifiable technique for recording dimension changes. Recently, we have improved our ultrasonic transit time technique so that we can obtain continuous records of the diameter of the cava in awake, exercising animals. These records can be calibrated at any time.

A major problem in defining active changes in tone in an intact animal is that the baseline information of pressure and radius represent only a single point in a pressure-radius plot. Some intervention is necessary to produce an array of pressure-radius relationships that would permit the derivation of a slope. In the experiments reported here, an occlusion device was used to generate a pressure-radius curve for the control state. These slopes can be compared with those from other intervention such as exercise or catecholamine infusion.

Materials and Methods
Nine dogs of random breed and sex weighing 18 to 24 kg were studied. Under pentobarbital anesthesia (30 mg/kg iv), with respiration supported by a Palmer respirator, a right thoracotomy was performed under aseptic conditions. Piezoelectric crystals 5 mm in diameter were placed on opposite surfaces of the superior vena cava at the level of the entrance of the azygos vein. The crystals were lead zirconate-titanate, with convex acoustical lenses on the vein side and a small strip of thin Silastic sheet on the outer side to prevent adhesions. The Silastic strips were sutured to the caval adventitia with 6-0 atraumatic sutures. A Silastic cannula was introduced into the azygos vein and advanced into the cava at the level of the crystals. A flat Silastic balloon was placed over the right side of the cava and the tube brought out through the skin to the...
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Original analog record produced by occlusion of the superior vena cava (SVC). Zero flow is indicated, but the flow was not calibrated in this chronic experiment. Left ventricular stroke volume decreased very slightly 6 seconds after the occlusion began, but the arterial pressure did not fall.

The subscapular area. An occlusive device was placed around the lower superior vena cava just above the junction with the right atrium. The occluder was constructed of thin Silastic sheets reinforced with Dacron on the outer circumference, causing inward compression of the caval wall when inflated. To relate effects of caval dynamics to the cardiovascular system, lightweight flow probes for a pulsed ultrasonic flowmeter were placed on the high superior vena cava and on the root of the aorta, and a Silastic cannula was placed in the internal mammary artery for pressure.

After 5 days or more for recovery, the animals were studied. Occlusion of the cava by inflation of the Silastic cuff was maintained for less than 5 seconds to avoid feedback, since the time constant for neurally mediated changes in most vessels is on the order of 10 to 20 seconds (2, 3). The pressure and diameter data generated by the occluded venous return represented a wide range for this relationship at the time of occlusion. Following a recovery period of 20 minutes, further experimental procedures were performed, including fright, exercise on a treadmill, and infusion of catecholamines. Control occlusion data were obtained before each intervention, but not during the intervention, since the experimental procedure itself generated a sufficient spread of data points for comparison with the control occlusion curves.

### Results

Figure 1 is representative of the analog recordings of the control occlusion. Figure 2, a pressure-radius occlusion curve, was obtained on-line using an x-y plotter and indicates the characteristic presence of hysteresis, with the descending limb at a lower pressure for a comparable radius. The slopes and origins of control data varied considerably from one animal to another, and even in the same animal. Variation in the same animal represented, in addition to "physiologic variation," variation in the conscious animal's response to the experimental laboratory. In some instances the control occlusion had a relatively steep pressure-radius slope, suggesting increased adrenergic activity before the intervention.

Figure 3 is a plot of the ascending limbs of pressure-radius plots from an occlusion at rest.
An x-y plot of pressure-radius obtained on-line by occlusion of the superior vena cava, demonstrating hysteresis of the loop. The occlusion time was 5 seconds. Arrows indicate the temporal sequence of the loop. The large excursions near the origin represent inspiratory effects.

(open circles) compared to data points generated by intravenous infusion of 1 μg/kg/min of norepinephrine, without occlusion. The duration for the two plots is necessarily different, since the occlusion lasted only 5 seconds, whereas the sigmoid curve of norepinephrine infusion represents a 3-minute period, sufficient time to allow considerable stress relaxation to occur, a fact which makes the steeper slope produced by norepinephrine even more significant. A simple sigmoid curve was present in only four of nine animals with norepinephrine, although eight of the nine had evidence of constriction. Four animals showed an actual decrease in diameter (Fig. 4). The one animal which failed to demonstrate any change in pressure-radius relationships with norepinephrine was presumably constricted in the "control" state.

Isoproterenol also produced constriction of the superior vena cava in eight of ten experiments in nine animals. In three instances, the diameter became smaller, as in Figure 4. Epinephrine produced constriction in all five instances it was given.

Exercise of 3 miles per hour on a 5% grade for 10 minutes, using a gradually starting treadmill, was successfully carried out in five animals. In two animals a sigmoid curve was produced; in one animal the diameter became smaller, and two showed no significant deviation from the control occlusion plot. Fright invariably produced definite evidence of active constriction of the cava.

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Original analog record during an infusion of epinephrine, 1 μg/kg/min. Note the decrease in caval diameter coincident with a rise in distending pressure. The increase in heart rate and aortic flow velocity (not stroke volume) occurred at the same time as the caval changes, indicating that the latter were a direct effect of the epinephrine, not reflex effects.

Discussion

The present method permits precise measurements of pressure-radius relationships in intact, unanesthetized animals. The method can be used without the acute stress of surgery and allows studies under physiologic stresses and strains. Even so, there were several instances in which the control state showed a steep pressure-radius curve, and experimental intervention failed to cause further steepening of the curve. This suggests that undetected increased adrenergic effects may be present at times in the awake animal.

Although peripheral veins above the heart level may collapse, this has not been proved to occur in the superior vena cava of the dog with closed chest. We placed crystals at different sites around the circumference of the superior vena cava and found no differences between sites after recovery from the thoracotomy. Similarly, flow is not intermittent in the superior vena cava (Fig. 1) as would occur with intermittent collapse, nor are there major variations in the diameter of the superior vena cava during respiration. In fact, spontaneous strains observed in all of our studies were considerably less than 5%. The dog, of course, ordinarily operates with the trunk level, and the hydrostatic level of the superior vena cava is not significantly different from that of the right atrium.

When the superior vena cava is occluded under the influence of norepinephrine, the pressure-radius curve approaches the same elastic limit of the control curve at unphysiologic pressures. This has been reported previously by Alexander (4) who used different techniques, although others have claimed a lesser distensibility for a constricted vein even at high levels of pressure. Our data indicate that it is easier to demonstrate changes in tone of the veins at physiologic stresses and strains.

The mechanism of constriction of the superior vena cava during exercise is not clear from our studies. Lesh and Rothe found relatively little change in the capacity of veins of muscle with sympathetic nerve stimulation (5), consistent with the finding that veins contain relatively fewer adrenergic nerve endings than arteries (6). We favor circulating catecholamines as the mechanism of venoconstriction but have no data to support this at present.
The constrictor response of the superior vena cava to exercise was not found in each case, possibly because of adrenergic activity in the control period, or it may reflect lesser degrees of physiologic stress with the moderate levels of exercise used. In a previous study of splanchnic constriction in exercising dogs, we found that this level of exercise could be initiated and maintained without contraction of this major reservoir in the dog in one-half the experiments (7).

The usual response, constriction of the superior vena cava to exercise, was similar to that with intravenous isoproterenol. As Shepherd suggested (8), venous constriction is a "logical accompaniment of increased cardiac output and decreased total systemic vascular resistance" with either muscular exercise or isoproterenol. Others have reported that isoproterenol dilates peripheral veins (9), but our results on the superior vena cava are similar to those of Kobor et al. (10), who found venoconstriction with either alpha- or beta-receptor stimulation.

References
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