Simultaneous Pressure, Flow and Diameter of the Vena Cava with Fright and Exercise

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ABSTRACT

The diameter, distending pressure and flow in the superior vena cava and aortic flow were recorded simultaneously in unanesthetized dogs. Atrial systole produced a regurgitant flow pulse and an increase in pressure and diameter. Ventricular systole produced a sharp decrease in caval diameter and a large increase in flow. A second flow pulse occurred during ventricular diastole. Inspiration accelerated flow in the cava. During exercise, the caval diameter invariably decreased. Venoconstriction, however, could be unequivocally demonstrated in only 26% of the treadmill runs. In 88% of 33 recorded treadmill runs, the flow in the vena cava increased before the heart rate increased which, in turn, preceded the increase in aortic stroke volume. Frightening the animal produced a prompt decrease in caval diameter and distending pressure; this gave way to increased pressure, but without a corresponding increase in diameter. Epinephrine and norepinephrine produced a sustained increase in distending pressure and an initial decrease and a more sustained increase in diameter. Isoproterenol produced tachycardia and a decrease in distending pressure and diameter. Acetylcholine caused an initial bradycardia which was associated with an increase in diameter and pressure in the vena cava followed quickly by prolonged tachycardia which was associated with a decrease in pressure and diameter.

ADDITIONAL KEY WORDS cardiac output venous return
venoconstrictor drugs tachycardia acetylcholine
 catecholamines isoproterenol unanesthetized dogs

An increase in venous return within a few seconds of the onset of exercise is almost certain, considering the volume of blood immediately available to the right ventricle.1 When a steady state has been achieved, the venous return reflects simply the increased cardiac output, but it is not certain whether the venous return passively follows the increased cardiac output from the very beginning of exercise. Although venoconstriction has been demonstrated in acute experiments involving relatively gross perturbations of the circulation in animals,2–4 venoconstriction with exercise has been demonstrated only in the human forearm.5,6 There are no reports on the effects of exercise on "tone" in the vena cava, the immediate tributary to the right atrium.

We have studied changes in diameter of the superior vena cava in relation to its distending pressure and also the changes of caval flow in relation to aortic flow in various conditions, particularly fright and exercise. Our major objectives were to determine whether active constriction of the vena cava occurs and whether the increase in caval flow with exercise precedes or follows the increase in aortic flow. In addition, we determined the interrelationships of pressure, diameter, and flow in the cava with the heart beat and respiration.

Methods

Ten dogs of random breed and sex, weighing

Circulation Research, Vol. XIX, July 1966
18 to 25 kg were studied. Under aseptic conditions, and under general anesthesia (pentobarbital, 30 mg/kg iv), a right thoractomy was performed. Transducers were implanted for the simultaneous recordings of changes of diameter, distending pressure, and blood flow in the superior vena cava and the aortic blood flow.

To measure changes of caval diameter, mutual inductance coils were sutured onto the adventitia with 6-0 nylon sutures on opposite sides of the vena cava. Each coil was about 7 to 8 mm in diameter and consisted of 200 turns of 1 mil enamel-covered copper wire. One of the coils was activated by 100 kC current; the voltage induced in the secondary coil was amplified, after demodulation, and recorded. The output in relation to a wide range of separation of the two coils is nonlinear, although over the short range encountered in the present study, the nonlinear effects are minimal. The voltage induced in the secondary coil is inversely proportional to the separation of the two coils; the recording polarity is reversed, so that an upward deflection indicates greater separation of the coils, or an increase in diameter of the superior vena cava.

To measure flows, one ultrasonic transducer was placed on the superior vena cava above the entrance of the azygous vein and another on the descending thoracic aorta. The flows were measured with a transistorized, pulsed ultrasonic flowmeter. Zero flows (fig. 1) were obtained briefly by injecting 2 to 3 mg acetylcholine iv to produce transient cardiac arrest. Calibration was not done since we were interested chiefly in relative changes of flow, and in timing of these changes.

To measure pressures, a silastic catheter was inserted into a tributary of the azygous vein and advanced into the midstream of the superior vena cava, with the tip of the catheter at the level of the mutual inductance coils. A silastic balloon was positioned in the pleural cavity overlying the superior vena cava. After recovery from the operation, the venous and the intrathoracic catheters were connected to opposite sides of a Sanborn differential pressure gauge for measurement.

![Figure 1](image-url)

**FIGURE 1**

*Effects of cardiac and respiratory cycles on caval dynamics and on flow in the descending aorta, as modified by 3 mg of acetylcholine. The terminal part of the record was obtained at paper speed of 1 mm/sec. "Eff. Vena Cavai Pressure" (measured in mm Hg) refers to the effective or distending pressure of the vena cava, obtained with a differential pressure transducer, applying the caval pressure on one side of the diaphragm and the intrathoracic pressure on the other. Zero flows are indicated for aortic and caval flow. Calibration of caval diameter omission here since the absolute diameter is impossible to determine directly with the mutual inductance method (see text).*

Circulation Research, Vol. XIX, July 1966
of the distending ("effective") pressure of the superior vena cava. For studies involving drugs, arterial pressure was recorded by intra-arterial needle. All pressure transducers were positioned at the midthoracic level (sternal-vertebral direction).

All animals were studied four to ten days after operation. Exercise was performed on a variable speed, gradually starting treadmill at three miles per hour on a 5% grade for ten minutes if tolerated. When possible, the animals selected for study were those not excessively alarmed by the treadmill. The runs were repeated frequently in an effort to separate the effects of exercise and fright. In separate experiments, fright was deliberately induced by explosion of a firecracker or by other sudden loud noise.

Several vasoactive drugs were infused in unanesthetized dogs or dogs lightly anesthetized with morphine 2 mg/kg, IM, and pentobarbital 15 mg/kg, IV. Epinephrine, norepinephrine and isoproterenol were given at a rate of 2 μg/kg in a single intravenous injection and in some dogs at a rate of 2 μg/kg per minute for three minutes. The period between administration of each drug was at least 15 minutes. In all cases, the variables had returned to control levels prior to injection of the next drug.

For timing of normal events of the cardiac and respiratory cycles, an electrocardiogram and phonocardiogram (Sanborn, contact) were used for reference.

Results

Figure 1 shows a typical record of the diameter, flow and distending pressure of the vena cava in relation to respiration and to aortic flow. In this instance, acetylcholine had been given in order to produce transient cardiac arrest, which allows identification of zero flow. The profound bradycardia immediately following the arrest, and the succeeding tachycardia produce considerable changes in the timing and morphology of the wave forms.

Although the mutual inductance coils used for recording changes in the diameter of the vena cava do not permit quantification, an estimate of the significance of the changes can be made by comparison with a more precise method of measuring distance. In one animal, simultaneous recordings were obtained with mutual inductance coils and a modified sonar system, and the two records were indistinguishable. The sonar system is unsatisfactory in exercise studies because the critical alignment of the miniature barium titanate crystals frequently cannot be maintained, but the sonar system permits quantification which can be extrapolated to the mutual inductance records. Caval pulsations secondary to cardiac systole averaged 0.35 mm, on a cava of 18.5 mm diameter, or approximately 2% of the diameter. Changes observed in experiments could then be compared to the pulsations secondary to cardiac systole for an assessment of the significance of diameter changes.

The results of the studies are reported according to the effects of the cardiac cycle, respiration, exercise, fright and vasoactive drugs.

Effects of the Cardiac Cycle

Several hundred cardiac cycles from 30 technically satisfactory experiments were inspected for timing and morphology of the wave forms. The characteristic changes in diameter, flow and pressure of the vena cava with the phases of the cardiac cycle in the unanesthetized, resting dog are diagramed in figure 2. The precise timing of events and relative magnitudes of the component waves varied from animal to animal, and in the same animal depending upon cardiac and respiratory rate.

Atrial Systole

Simultaneous with the A wave of the venous pressure, an increase in diameter occurs in the vena cava. Shortly thereafter, flow in the vena cava decelerates, to the extent of reversal of flow, shortly after the inscription of the peak of the A wave of the venous pressure.

Ventricular Systole

The diameter of the vena cava decreases sharply during early ejection, and there is no counterpart of the C wave which is seen in the caval pressure tracing in figure 2. This abrupt collapse in dimension of the cava is followed by rapid distention later in the ejection period, corresponding to the V wave of the pressure record. The vena cava flow, on the other hand, accelerates from the onset of the isometric contraction, and rises throughout the ventricular ejection period, reaching...
VENA CAVA STUDIED DURING FRIGHT AND EXERCISE

Characteristic morphology and timing of events in the superior vena cava during the cardiac cycle. ECG and phonocardiogram (PCG) are presented for timing. This diagram represents a synthesis from several hundred records, which showed considerable variation, particularly with respect to amplitude.

Ventricular Diastole

The peak of the v wave of the venous pressure occurs immediately after the point of maximal distension of the vena cava. Thus, after the second heart sound, all three curves decline. Pressure, diameter, and flow reach a nadir at approximately the same instant, slightly beyond the period of rapid ventricular filling. The caval flow increases to a second peak at about mid-diastole. The second flow pulse may be of more or less amplitude than the systolic peak, and the two pulses may fuse with more rapid heart rates. The caval pressure and diameter increase slowly as flow declines in late diastole.

EFFECTS OF HEART RATE

When the heart rate increased, the diastolic flow peak in the vena cava which occurred at slower heart rates (fig. 2) became less distinct, largely as a result of fusion with the large systolic flow wave. Also, the regurgitant pulse with atrial systole disappeared. These changes in the vena cava flow within the cardiac cycle were seen in exercise and when the heart rate was modified with acetylcholine.

EFFECTS OF RESPIRATION

Inspiration usually produces an obvious acceleration of blood flow in the superior vena cava (fig. 1). The intraluminal pressure in the vena cava invariably falls with inspiration, but the diameter increases in only one-half the animals. The distending pressure (intraluminal minus pleural pressure) frequently does not change with respiration in those instances in which the pressure in the vena cava falls to the same extent as the pleural pressure. In addition, the normal increase in heart rate with inspiration tends to deplete the volume of blood in the vena cava.

EFFECTS OF EXERCISE

The dimensional changes in the superior vena cava were recorded satisfactorily during treadmill exercise 50 times in seven trained animals. A sustained decrease in the diameter of the vena cava was recorded in all these instances (fig. 3). In 39 instances in which the effective vena cava pressure was recorded, an average decrease of 2.6 mm Hg (range 0.5 to 6 mm Hg) occurred in 74% (29 instances). In 21% (8 instances) the effective venous pressure rose during exercise by an average of 4.2 mm Hg (range 1 to 8 mm Hg).

In two instances the venous pressure did not change but there was a simultaneous decrease
Effects of exercise on a treadmill. Sharp decrease of effective venous pressure accompanies onset of exercise, followed by almost complete recovery, whereas there is a sustained drop in the caval diameter. Note that the increase of flow in the vena cava precedes the increase of aortic flow by four to five seconds.

Exercise on a treadmill, recorded at paper speed 5 mm/sec. Although the caval diameter is substantially diminished with exercise, the effective pressure is also reduced, thus making a definite statement about vasoconstriction difficult without quantitative diameter measurements. Heart rate does not increase for two seconds after caval size decreases and caval flow increases, while aortic stroke volume does not increase above the control level for eight seconds.
VENA CAVA STUDIED DURING FRIGHT AND EXERCISE

of the vena cava diameter. Thus, in 26% of the instances the venous pressure rose or did not change in the presence of a decreased diameter of the vena cava with exercise.

Instantaneous changes in vena cava flow and aortic flow induced by exercise were recorded simultaneously in 33 instances. In 88% of the records with exercise (29 instances), the instantaneous flow in the vena cava increased before the increase in aortic stroke volume by an average of 8.7 seconds (range 4 to 15 sec, fig. 4). In only 9% of the runs (3 instances) the superior caval (SVC) flow and the aortic stroke volume increased simultaneously. The heart rate accelerated, on the average, 1.5 seconds (range 0.5 to 3 sec) after the increase in SVC flow, but before there was a definite increase in aortic stroke volume. Thus, the increase in venous return at the onset of exercise preceded the increase in heart rate and this, in turn, preceded the increase in aortic stroke volume.

EFFECTS OF FRIGHT

When fright was deliberately induced with a firecracker explosion (at least once in each of the 10 dogs) there was an immediate decrease in SVC diameter, an increase in SVC flow, and an increased heart rate, followed by an increase in aortic stroke volume (fig. 5). There was an initial drop in venous pressure, followed by a sustained increase in distending pressure, whereas the caval diameter recovered to control level quickly and did not dilate with the increased distending pressure, indicating venoconstriction. The effects of fright cannot be totally free from the effects of exertion. Although the animals were loosely restrained, some muscular activity, such as trembling, followed the startle response.

EFFECTS OF NOREPIEPHRINE AND EPINEPHRINE

When a single injection of 40 μg of either

FIGURE 5
Effects of fright produced by the explosion of a firecracker. There is a simultaneous fall in pressure and diameter of the vena cava, but an overshoot of pressure, while the diameter returns only to its base line, indicating venoconstriction. Caval flow rises immediately, at approximately the same time the heart rate increases. However, aortic stroke volume actually drops with the increased rate and does not increase until four seconds after the cava decreases in diameter.

FIGURE 6
Effects of an intravenous injection of norepinephrine, 2 μg/kg. Caval diameter decreases initially, accompanied by an increase in flow but an increase in effective pressure.
of these two drugs was given, two types of responses were recorded in the diameter of the vena cava. In 47% (18 instances in 8 dogs), a biphasic, negative-positive change in the caliber of the vein was found (fig. 6). This initial decrease lasted for an average of 14 seconds (range 3 to 28 sec), and occurred at the time when the effective venous pressure was rising, suggesting that venoconstriction had taken place. The continuous elevation of the effective venous pressure, however, seemed to overcome this initial venoconstriction and induced a subsequent increase in the vena caval diameter, paralleling approximately the increase in venous pressure. In the other 20 instances (53%) a single injection of 40 μg of norepinephrine or epinephrine failed to induce the initial decrease in the diameter of the vena cava. However, the venous pressure in these 20 records started to rise 4 to 10 seconds before the increase in caval diameter. This brief period of rising venous pressure without a change in the caliber of the vein indicates initial venoconstriction.

When norepinephrine was infused slowly in 3 animals during a 2- to 3-minute period and using a greater dose (2 μg/kg/min in 3 min) a minimal increase occurred in the dimensions of the vena cava in contrast to a large, sustained increase in the venous pressure.

EFFECTS OF ISOPROTERENOL

Isoproterenol was given in 15 instances to 8 dogs. Tachycardia and an increase in cardiac output occurred invariably (fig. 7). Caval diameter decreased in all but two instances, in association with a fall in pressure of 2.7 mm Hg average (range 1.5 to 5 mm Hg). In the two instances in which the diameter increased, there was an associated rise in pressure in the vena cava. Initial, transient increases in both pressure and diameter were observed in a few instances.

EFFECTS OF ACETYLCHOLINE

Acetylcholine was given at least once during each experiment to establish zero flow levels. The intravenous dose was very large, 3 to 4 mg, sufficient to produce transient cardiac arrest (fig. 1), so that the observed effects reflect predominantly cardiac responses. In 15 experiments in 7 dogs, all of the variables were recorded satisfactorily. During the initial bradycardia, the diameter and pressure of the vena cava invariably increased, along with the decrease in flow in the cava. During the ensuing prolonged tachycardia, both pressure and diameter decreased, as the flow increased.

FIGURE 7

Effects of a slow intravenous injection of isoproterenol showing initial slight increase in both pressure and diameter of the vena cava. As tachycardia develops 35 seconds after the infusion is started, pressure and diameter both fall. Since the two are more or less parallel, no conclusion as to venoconstriction can be drawn.
Discussion

CARDIAC CYCLE

The effects of the cardiac cycle on pressure and flow records of the superior vena cava were previously reported by Brecher for acute experiments. The dimensional changes of the vena cava with the cardiac cycle are similar to those described by Irisawa et al. Although the timing and magnitude of the fluctuations in pressure, flow and diameter were very variable in different animals, the general relationships shown in figure 2 were relatively constant in animals with slow heart and respiratory rates.

The marked acceleration of caval flow during ventricular systole accompanied by a fall in pressure and diameter agrees with Brecher’s conclusions that the ventricle has some ability to draw blood into the atrium. This function may become important with marked tachycardia, when the diastolic filling interval of the ventricle becomes the limiting factor in cardiac output. Enhanced atrial filling by ventricular systolic suction should enhance ventricular filling when filling time is critically reduced.

RESPIRATION

The effects of inspiration upon the vena cava are variable, depending upon the degree to which the fall in intrathoracic pressure is transmitted to the vena cava. In some animals with slow respiration and heart rate, inspiration produced no measurable change in the distending pressure of the superior vena cava (intraluminal minus pleural pressure). In less than one-half the animals, the pleural pressure fell more than the intraluminal pressure, thereby increasing the distending pressure of the vena cava and the caval diameter. On the other hand, the intraluminal pressure invariably fell with inspiration compared to atmospheric pressure creating a pressure gradient favorable to flow into the intrathoracic vessels and chambers.

ACTIVE VENOCONSTRICTION

In the absence of quantitative diameter measurements, venoconstriction can be demonstrated by 1) a decrease in diameter in the presence of an increased or unchanged distending pressure of the vena cava, or 2) an unchanged diameter in the presence of increased distending pressure. These combinations were not easy to elicit in the vena cava, even with catecholamines. With noradrenaline, for example, the distending pressure invariably rose, and the caval diameter increased; definite venoconstriction could be demonstrated only in those instances that presented an initial, transient decrease in diameter (47% of the experiments).

Evidence for spontaneous venoconstriction was more scarce. Although the caval diameter decreased with exercise in every instance, the distending pressure also decreased in 74%, and in only 35% of the treadmill runs was there evidence of venoconstriction. There were many other instances in which the degree of change in diameter appeared to be much greater than the degree of pressure change, suggesting venoconstriction, but this inference is not warranted without quantitative diameter measurements. With fright, however, venoconstriction was regularly evident, since a sustained increase in vena caval pressure occurred with no increase in diameter. Although muscular activity undoubtedly occurred with fright and may have enhanced venous return by the “muscle pump” effect, this is not germane to the conclusion of vasoconstriction as defined above. If caval pressure is elevated by a peripheral mechanism such as venular constriction or muscle pumping, the caval diameter will increase unless there is a change in tone.

INCREASED RETURN PRIMARY OR SECONDARY TO INCREASED OUTPUT?

Krogh postulated, a priori, that for an increase in cardiac output there must be a preceding increase in venous return. Indeed, in 88% of our records of the onset of exercise, the flow increased and the diameter decreased in the superior vena cava prior to the increase in heart rate. With increased heart rate, the aortic stroke volume either remained constant or actually fell for three or four beats, and then the aortic stroke volume...
recovered and usually increased over the resting stroke volume, an average of eight seconds after the onset of exercise. This differs from the results of Franklin et al. who were unable to demonstrate an increase in caval flow prior to an increase in left heart output.19

References
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Circ Res. 1966;19:42-50
doi: 10.1161/01.RES.19.1.42
Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4571

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