Response of the Heart to Increased Peripheral Resistance

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The recent studies of Sarnoff and his collaborators\(^1\) indicate that the level of pressure in the carotid sinuses reflexly modifies myocardial contractility. The left ventricular response to the generalized augmentation of peripheral resistance engendered by carotid sinus hypotension should therefore be affected by such reflex inotropic influences. The present study was conducted to assess the role of the baroreceptor reflexes in the ventricular response to increased peripheral resistance. Left ventricular performance was evaluated over comparable ranges of augmented resistance, but under conditions in which the level of pressure in the carotid sinuses was either elevated, normal, or diminished.

**Methods**

Experiments were performed upon 10 mongrel dogs weighing 17.2 ± 5.0 (SD) kg. In seven experiments, pentobarbital, 30 mg/kg, was administered intravenously. In three experiments, the dogs were anesthetized with the combination of agents employed by Sarnoff and his collaborators,\(^2\) i.e., morphine sulfate, 2 mg/kg, intramuscularly, followed in 30 minutes by a warmed solution of chloralose (60 mg/kg) and urethane (600 mg/kg), intravenously. Intermittent positive pressure breathing was instituted. An incision was made in the fourth left intercostal space. The ascending aorta was freed from the pulmonary artery with the minimum amount of dissection necessary to permit application of a C-core electromagnetic flowmeter probe\(^3\) about the origin of the aorta. Heparin, 3.4 mg/kg, was given intravenously to prevent blood coagulation. A catheter was passed into the left atrium via a pulmonary lobular vein for pressure recording. A T-cannula was inserted into one common carotid artery to permit measurement of pressure, without interfering with the normal flow of blood through the vessel. The left subclavian artery was ligated near its origin; a short, rigid catheter was passed into the proximal segment to permit aortic pressure recording. Screw clamps were placed around the brachiocephalic artery and the descending thoracic aorta just beyond the origin of the subclavian artery. Pressures distal to the aortic clamp were measured from a cannula in the femoral artery. Methods for recording phasic pressures, left ventricular outflow (minus coronary blood flow), stroke volume, work, and power have been described previously.\(^4\)

**Results**

Segments of records which were obtained during a typical experiment are reproduced in figure 1. Cyclical changes were observed with respiration, and each segment was selected from a corresponding portion of the respiratory cycle. The figure reveals the effects of three different degrees of constriction of the brachiocephalic artery. From a control arterial pressure of 112/90 mm Hg (segment a), progressive constriction of the brachiocephalic artery diminished the mean pressure in the carotid artery to 87, 48, and 24 mm Hg, respectively, with a pronounced damping of the pulsations (segments b, c, d). Associated with the decrease in pressure in the carotid artery, there was an increase in pressure in the aorta and femoral arteries. Only negligible changes in left atrial pressure occurred. Peak aortic flow showed only a slight tendency to increase with progressive constriction, and this persisted after release (segment e). The variations of the stroke volume were parallel to those of peak aortic flow. There was a pronounced increase in peak left ventricular power and stroke work, related to the degree of constriction of the brachiocephalic artery. From a control value

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Circulatory response to graded constriction of the brachiocephalic artery in a typical experiment. Segment a represents the control state; segments b, c, and d, progressively more severe constriction of the brachiocephalic artery; and segment e, release of constriction.
of 10.4 mm Hg-liters/sec, the peak power increased to 13.6 with slight constriction, and to 15.2 with moderate and severe constriction, and fell to 11.2 during the recovery period. Similarly, the control stroke work was 1.75 mm Hg-liters. It increased to 2.25, 2.55, and 2.60 mm Hg-liters with progressive constriction, and returned to 1.80 in the recovery period. Heart rate did not vary appreciably during these procedures.

Immediately after these tracings had been obtained, three different grades of constriction of the descending aorta and of the aorta plus brachiocephalic artery were produced in alternating sequence. The results of these procedures were also similar to those obtained in the other experiments of this series. Therefore, they will not be described separately, but are included in the composite data depicted in figure 2. In this figure, the data are presented in terms of per cent of control, and they are compared over similar ranges of augmented total peripheral resistance (TPR).

In the resistance range from 100% to 150%, the mean resistance was 130% ± 3.0% (SE) for aortic constriction, 127% ± 3.4% for brachiocephalic constriction, and 135% ± 4.6% for the combined compression. In the range from 151% to 200%, the values were 176% ± 9.0%, 175% ± 6.7%, and 163% ± 3.5%, respectively. In several experiments, changes in resistance in excess of 200% were produced, but the data are not sufficiently abundant to be included.

For comparable changes in TPR, mean arterial pressure was elevated to a greater extent by brachiocephalic constriction than by either of the other procedures over both
ranges of TPR. With aortic constriction, the elevations in mean carotid pressure were identical with those in mean aortic pressure. With brachiocephalic constriction, mean carotid pressure was reduced to 77.4% ± 9.4% of control in the lower range of elevated resistance, and to 57.0% ± 7.7% in the higher range. When brachiocephalic constriction was superimposed upon aortic compression, the mean carotid pressure was remarkably close to the control pressure levels.

Stroke volume was reduced to 91% ± 2.9% and 86% ± 3.9% of control by aortic and combined constriction, respectively, in the lower range of increased TPR, and to 76% ± 7.7% and 78% ± 3.4% in the upper range. With compression of the brachiocephalic artery alone, on the other hand, stroke volume did not vary significantly from the control level. Heart rate did not change appreciably in these experiments, so the variations in stroke volume represent the behavior of cardiac output as well.

Stroke work and peak left ventricular power did not differ significantly from the control levels by aortic or combined constriction. However, both of these variables increased appreciably during constriction of the brachiocephalic artery alone, and the changes were more pronounced in the higher range of augmented TPR.

The mean left atrial pressures averaged 7.2 ± 1.2 mm Hg during the control period. The changes with increased TPR represented only a few mm Hg, but when computed in terms of percentage of control, the variability was appreciable. In general, mean left atrial pressure increased from 20% to 40% with aortic or combined constriction, but did not vary significantly from control levels with brachiocephalic constriction. The changes in mean pressure were paralleled by changes in end-diastolic pressure.

In all experiments, after these data had been obtained, the vagi were sectioned bilaterally. At the beginning of this study, it was suspected that changes in heart rate might arise during the various experimental maneuvers, and that vagotomy would obviate this effect. In these experiments, however, heart rate did not vary appreciably. The response of the heart to aortic, brachiocephalic, and combined compression was similar after vagotomy, and therefore the additional data will not be presented.

**Discussion**

In the present study, the response of the left ventricle to augmented peripheral resistance was dependent upon the method of altering impedance. With compression of the aorta or of the aorta plus brachiocephalic artery, the elevations of mean arterial pressure were usually attended by approximately equal reductions in stroke volume. Stroke work and peak power did not vary significantly from the control levels. Since these variables do diminish appreciably as the immediate response to equivalent augmentations of resistance in isolated heart preparations,4,5 the maintenance of control levels of work and power in the more intact preparation, employed in this study, indicates the supervision of certain adaptive mechanisms. Elevation of the left atrial pressure signifies that the Frank-Starling mechanism6,7 probably plays a prominent role. Whether homeometric autoregulation2,5,8 is also invoked cannot be ascertained from these data.

The response to brachiocephalic constriction was considerably different from that to aortic or combined compression. For equivalent increases of TPR, stroke volume remained at control levels, and mean arterial pressure was augmented to a greater extent (fig. 2). Stroke work and peak power were considerably enhanced, while left atrial pressure was not significantly elevated above control levels. These differences in response to brachiocephalic constriction are probably related to the level of pressure in the carotid sinuses, but may also depend upon differences in arterial compliance. The relative importance of these factors cannot be ascertained from the present data.

The increased TPR observed with brachiocephalic artery constriction results from gen-
generalized arteriolar vasoconstriction. Hence, arterial compliance is distributed over the entire arterial system. With progressive aortic or combined compression, on the other hand, the critical elastic component becomes more and more restricted to that segment of aorta proximal to the constricting clamps. The ability of the ventricle to eject blood against an increased resistance is determined to a considerable extent by the compliance of the arterial system into which it is pumping. Also, for a given cardiac output, the heart operates from a lower end-diastolic pressure and volume when pumping into a compliant system than into a rigid system. 

Brachiocephalic artery constriction probably elicits reflex inotropic effects associated with the reduction in pressure in the carotid sinuses, although this has recently been contested. The effects observed in the present study cannot be ascribed to cerebral ischemia, since in the range of TPR from 100% to 150% (fig. 2), mean carotid artery pressure was only diminished to 77% ± 9.4% of control, a level sufficient to maintain adequate cerebral circulation. In many experiments (e.g., segment b of fig. 1), mean carotid arterial pressure was scarcely diminished, and the effects were evoked largely in response to the reduced pulse pressure. Furthermore, although contraction of a reactive venous reservoir has been described during carotid sinus hypotension, such a mechanism cannot account for the differences observed between brachiocephalic constriction and the other procedures. Left atrial pressures were certainly no higher with constriction of the brachiocephalic artery (fig. 2). Actually, when the data for the entire range of resistances were pooled, the left atrial pressures were significantly lower (P = 0.04) during brachiocephalic constriction than during aortic or combined constriction. It is likely, therefore, that the cardiac response to brachiocephalic compression is attributable, in part, to an inotropic effect based upon reflex sympathetic influences and the release of catecholamines by the adrenal medulla.

Changes in the resistance to left ventricular outflow were produced in the anesthetized, open-chest dog by constriction of the descending thoracic aorta, the brachiocephalic artery, or a combination of the two. With constriction of the brachiocephalic artery alone, left ventricular stroke work and peak power were considerably enhanced, left atrial pressure increased insignificantly, and cardiac output remained constant. With aortic or combined constriction, cardiac output diminished and left atrial pressure rose, but peak power and stroke work did not change significantly. The enhancement of peak power and stroke work by brachiocephalic constriction may be ascribed in part to the superposition of reflex and humoral inotropic mechanisms.

Summary

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