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JOURNAL OF THE AMERICAN HEART ASSOCIATION

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Circulation Research 1960, 8:549-552

doi: 10.1161/01.RES.8.3.549

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75214

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Regulation of Cardiac Output Through Stroke Volume

By HOMER R. WARNER, M.D., PH.D., AND ALAN F. TORONTO, M.D.

RECENT studies have clearly shown that the increased cardiac output that occurs during moderate exercise in mongrel dogs and untrained human subjects is associated with an increase in heart rate, but little or no change in stroke volume.^{1, 2} In the studies here presented, heart rate was controlled in dogs exercising on a treadmill in order to evaluate their ability to regulate cardiac output through alterations in stroke volume alone.

Methods

Seven untrained mongrel dogs were selected for this study on the basis of their willingness to run on a treadmill. Approximately 1 out of 10 dogs screened was suitable. Atrioventricular conduction was interrupted, using a modification of the surgical technic described by Taufie, Bashour, and Lewis.³ After anesthetizing the dog with an intravenous injection of sodium pentobarbital (25 mg./Kg.) his chest was opened through the right fifth intercostal space, using sterile technic, and 2 wires were passed through a puncture wound near the spine and sutured into the right ventricle. These were insulated, except where they contacted the ventricle. The other ends of the wires were connected to an electric stimulator in preparation for driving the ventricle after the A-V block had been produced. Tourniquets were loosely placed about the superior and inferior venae cavae and the azygos vein. Venous return was arrested for 1.5 to 2 minutes by tightening these tourniquets. During the period of occlusion, the right atrium was opened and an area about 2 mm. in diameter on the interatrial septum just below the tricuspid valve was destroyed by electrocautery. This usually resulted in a complete atrioventricular block and an idioventricular rate of

about 30/min. The ventricle was then driven by the stimulator at a rate of 90/min. After the chest was closed, a harness was placed on the dog and a small portable stimulator attached to it. This allowed maintenance of a normal heart rate when the dog was returned to his cage.

However, before the dog was returned, a right nephrectomy was done and permanent indwelling plastic cannulae were placed in the right renal artery and vein. These cannulae containing solid plastic styli were buried subcutaneously for easy accessibility. One to 2 weeks after the surgery, when the dog was ready to be studied, only local anesthesia was necessary to expose the cannulae. Through the venous cannula, a catheter could be passed into the right atrium for dye injection and pressure recording. The arterial cannula allowed passage of a catheter into the aortic arch for sampling of dye and recording of central aortic pressure pulse contours.

Cardiac output was measured by the indicator dilution technic. Fox green dye was injected into the right atrium while blood was withdrawn at a constant rate from the aorta through a cuvette oximeter for continuous measurement of dye concentration. Beat-by-beat changes in cardiac output were measured by the pulse contour method.⁴ Figure 1 shows a comparison of values for stroke volume, calculated by the pulse contour method and by the dye method in a resting dog at heart rates from 70 to 240/min. These data were obtained by recording from a resting dog, dye dilution curves via a needle in a femoral artery and aortic pressure via a catheter in the renal arterial cannula. These were recorded simultaneously on a multichannel magnetic tape. The pressure pulses during each dye curve were then fed from the tape to an analog computer, where the integrations required by the pulse contour method were performed. The use of electrical integration resulted in a significant improvement in the reproducibility of the pulse contour calculations. It should be emphasized that this pulse contour method measures only changes in stroke volume unless calibrated against one of the dye curves. Because the 2 methods agreed so well during the steady state, the pulse contour method was used to evaluate the effect of sudden changes in heart rate.

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Supported in part by Grants-in-Aid from the National Heart Institute (H-3607 [C-1]), and from the Utah Heart Association.

Received for publication December 21, 1959.

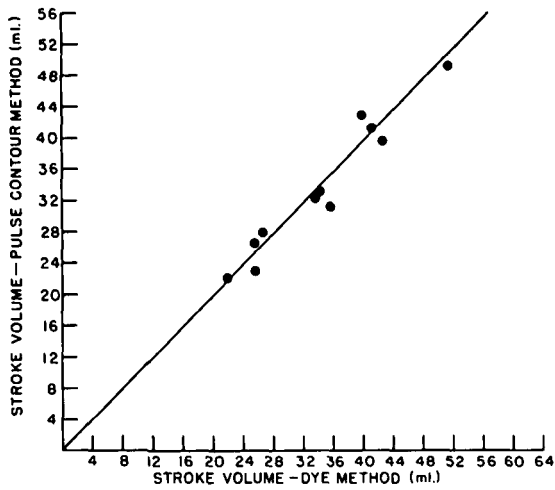


Figure 1

Simultaneous determinations of cardiac output by dye method (abscissa) and pulse contour method (ordinate) in a 26 Kg. dog at rest. Heart rate varied from 70 to 210/min.

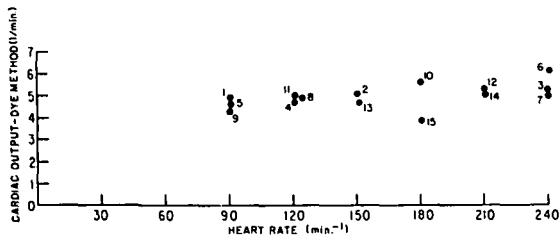


Figure 2

Fifteen determinations of cardiac output in an unanesthetized dog lying on a table. The numbers indicate the sequence of the determinations.

Results

Cardiac output as a function of heart rate in an unanesthetized dog at rest is plotted in figure 2. These 15 measurements were made at 2-minute intervals, the dye being injected 1 minute after each change in heart rate. The numbers indicate the sequence of the determinations. Under these circumstances, cardiac output was independent of heart rate over the entire range studied.

In figure 3, cardiac output is shown as a function of heart rate when the heart rate was changed at 10-second intervals. Here the pulse contour method was employed for the cardiac output measurements. Under these conditions, in which heart rate is changed at short intervals, cardiac output appears to decrease sig-

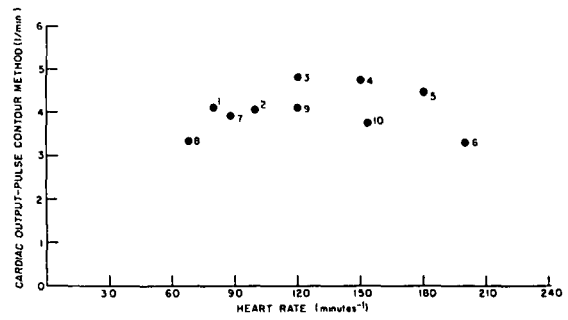


Figure 3

Effect of rapid changes in heart rate on cardiac output in a resting dog. The numbers indicate the sequence of the determinations.

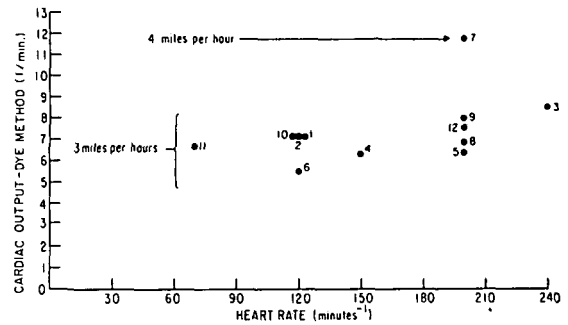


Figure 4

Effect of changing heart rate on cardiac output in an exercising dog. Weight, 26 Kg.

nificantly at both extremes of heart rate. The difference between this response and the one shown in figure 2 is thought not to be due to differences in cardiac output methods used, since good agreement between the methods was found during the steady state.

Other experiments were carried out with dogs exercising on a treadmill. The data shown in figure 4 were obtained from a dog trotting at 3 m.p.h. on a treadmill inclined to provide a 10 per cent grade. For each determination, the heart rate was set at the desired value and the dog was allowed to rest 3 minutes from the previous exercise run. Exercise was then begun and 2 minutes later dye was injected. At the end of the cardiac output determination exercise was stopped and the heart rate reset to the new level. Twelve such exercise runs were completed in the dog shown here. The numbers indicate the sequence of the determinations. Although there was some

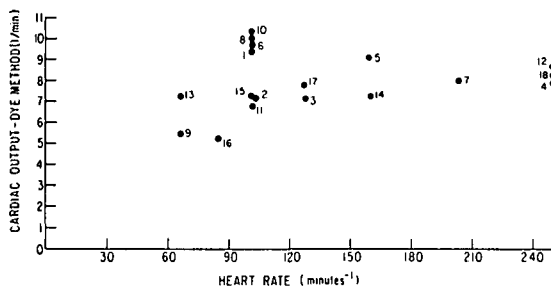


Figure 5

Effect of changing heart rate on cardiac output in an exercising dog. Weight, 28 Kg.

variation in cardiac output at a given heart rate, cardiac output did not systematically depend upon the heart rate under these conditions. Determination number 7 was obtained with the dog running at 4 m.p.h. and demonstrates that this dog is capable of increasing his cardiac output to a higher level in response to an increased demand.

In figure 5 is shown cardiac output data obtained from another dog, in which 17 exercise runs were carried out with the dog trotting at 3 m.p.h. on the treadmill. Here again, the dog's cardiac output by the dye method is independent of heart rate over a wide range. Attempts to evaluate the effect on cardiac output of rapid changes in heart rate during a single exercise run were unsuccessful, since the high fidelity pressure recordings required by the pulse contour method could not be obtained during exercise due to the artifact generated by catheter movement.

Stroke volume was calculated by dividing the cardiac outputs shown in figure 4 by the corresponding heart rates (fig. 6). Notice the large range of stroke volume achieved by this dog in maintaining a constant cardiac output during the exercise. Stroke volume at a heart rate of 70 is 3 times the stroke volume at the heart rate of 200.

Discussion

Activation of ventricular contraction by means of stimulating electrodes in the right ventricle differs in certain respects from activation through the normal mechanism. That this is so was clearly shown in the present studies by the fact that ventricular systole

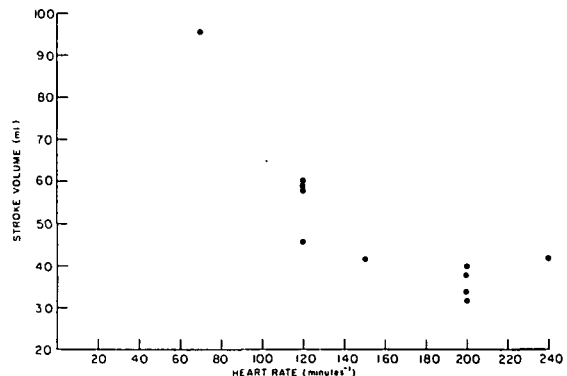


Figure 6

Stroke volume calculated from cardiac output and heart rate data shown in figure 4.

was significantly shorter at each heart rate than in a control animal at that rate. Also, in the present study the normal time-relationship between atrial and ventricular contraction was abolished. It seems unlikely, however, that either of these facts should detract from the basic observation presented, namely, that powerful control mechanisms exist which are capable of bringing about adjustments in stroke volume in response to a change in heart rate such that cardiac output will be held constant over a wide range of heart rates.

The present study was not designed to answer the question of how these adjustments in stroke volume are brought about. Although some progress has been made in several laboratories toward answering this question, it seems probable that a satisfactory quantitative understanding of the mechanisms involved can only be achieved when enough information is available regarding each of the component parts of this closed-loop circulatory system to allow simultaneous solution of all the component equations.⁵

Summary

Heart rate was controlled by direct stimulation of the right ventricle of a dog previously subjected to complete A-V block in order to study the effect of this variable on cardiac output. Measurements of cardiac output were made at various heart rates in unanesthetized dogs, both at rest and walking on a treadmill. Except at the extremes, cardiac

output was independent of heart rate at rest and during mild exercise. This finding emphasizes the fact that cardiac output may be regulated to provide required flow through changes in stroke volume alone, even though adjustment of heart rate is the usual means for obtaining this end.

Summario in Interlingua

Le frequentia cardiac esseva regulate per le stimulation directe del ventriculo dextere de un can previeamente subjeite a complete bloco atrio-ventricular, con le objectivo de studiar le effecto de iste variabile super le rendimento cardiac. Mesurationes del rendimento cardiac esseva effectuate a varie frequentias del corde in non-anesthiate canes, tanto in stato de reposo como etiam in ambulation in un machina de exercitio. Excepte sub conditiones extreme, le rendimento cardiac esseva independente del frequentia cardiac in stato de reposo e durante leve formas de exercitio. Iste constatation sublinea le facto que il es possibile regular le rendimento cardiac pro provider le requirite fluxo exclusivemente per alterationes in le

volumine per pulso, ben que le adjustment del frequentia cardiac es le methodo usual pro attinger iste objectivo.

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