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Research Article

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Pressure-Flow Studies in Man: Effect of Atrial Systole on Left Ventricular Function

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ABSTRACT In order to evaluate the effects of atrial contraction on left ventricular function, the pressure gradient technique was used to measure instantaneous aortic blood flow and pressure in nine patients, six having complete heart block and three having normal sinus rhythm. From these data both left ventricular stroke volume and stroke work were calculated. Ventricular rate was controlled by transvenous right ventricular pacing over a range of 50–158 beats/min. At each heart rate, beats which were not preceded by a P wave served as controls. The other beats were divided into six groups according to the duration of the preceding PR interval. The results indicated that stroke volume and stroke work were always affected similarly. In one patient the presence of a P wave did not alter the subsequent stroke volume significantly. In the other patients, beats preceded by P waves had stroke volumes greater than the controls. In general, there was no difference in stroke volume for beats preceded by a P wave having a PR interval within the range of 0.05–0.20 sec. As the PR interval lengthened beyond 0.20 sec stroke volume tended to decrease, especially at more rapid heart rates. The absolute increase in stroke volume after a beat preceded by a P wave (PR interval 0.05–0.20 sec) was quite variable among the patients. For a given patient the absolute increase in stroke volume was essentially independent of heart rate. The percentage change in stroke volume, however, was always greater as the heart rate increased.

These data indicate that in most patients atrial systole is important in augmenting ventricular stroke volume and stroke work especially at high heart rates, but the magnitude of these effects are quite variable among patients.

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INTRODUCTION

The extent to which a properly timed atrial systole can enhance left ventricular function by augmenting stroke volume has not been defined in man, primarily due to the technical difficulty encountered in accurately measuring phasic aortic blood flow. Experimental data in animals have shown that atrial contraction plays an important role in maintaining adequate cardiac function, especially at rapid heart rates (1–4). The present study was undertaken to further delineate the influence of a properly timed atrial systole on left ventricular function in man. The pressure gradient technique (5) was used to measure aortic blood flow continuously in nine patients having atrio-ventricular dissociation in whom the ventricular rate was altered over a wide range by electrical pacing. Since atrial systole occurred in a random temporal relationship to ventricular systole, the changes in left ventricular output secondary to variations in the timing of atrial systole could be determined.

METHODS

Phasic blood pressure and flow were recorded from the ascending aorta during the course of routine cardiac catheterization in nine adult male patients who had been admitted to the Durham Veterans Administration Hospital. The informed consent of each patient was given before this procedure. Six of these patients, ranging in age from 58 to 74 yr, exhibited complete heart block and three patients, ranging in age from 35 to 55 yr, had normal sinus rhythm. None had clinical evidence of congestive heart failure at the time of study. All of the patients with heart block had a history of Stokes-Adams attacks, three had a previous myocardial infarction, and another one had angina pectoris. Two patients with heart block manifested cardiomegaly

radiographically. One of these patients had a connective tissue disorder, most closely resembling polymyositis. Two of the three patients with normal sinus rhythm had diffuse myocardial disease and previously had congestive heart failure. The third patient was found to have an insignificant systolic murmur without other evidence of heart disease.

Phasic blood flow and pressure were measured in the ascending aorta by the pressure gradient technique (5, 6). This method is based on an approximate solution of the Navier-Stokes equations of fluid motion, which relate the axial pressure gradient to the blood flow (5). The instrumental techniques, manometric accuracy requirements, and calibration procedures used in our laboratory to obtain phasic flow in man have been previously described in detail elsewhere (6). The validity of this technique has been demonstrated in a flow generator (6), in the dog aorta (7), and in many studies in man, both in this laboratory (8, 9) and in others (10, 11).

A specially designed 6.5 French double-lumen catheter[1] having lateral pressure taps 4 cm apart was introduced percutaneously into the femoral artery and advanced to the ascending aorta. The lateral pressures were accurately measured with a transducer-amplifier system. The pressure difference obtained with an analog computer[2] was used to instantaneously solve the proper equation for phasic blood flow. Ascending aortic blood pressure was recorded directly from one lumen of the catheter. An ECG was obtained with an appropriate lead selected so that the P waves were easily detectable. All data were recorded on an optical recorder[3] at a paper speed of 100 mm/sec and on an FM electromagnetic tape recorder.[4]

The ventricular rate was controlled by right ventricular pacing, using a transvenous pacing catheter and an external pulse generator.[5] Patients in both groups were studied over a range of ventricular rates from 50 to 158 beats/min. One subject with heart block was paced at one rate only. In order to produce atrioventricular dissociation in the patients with normal sinus rhythm, the paced ventricular rate was faster than the sinus rate. In general the ventricular rate was increased in increments of 20 beats/min. At each new rate a period of 5 min was allowed to assure stabilization before recording of data.

In evaluating the data approximately 1200 separate beats were analyzed. The PR interval was measured from the onset of the P wave to the ventricular pacing artifact. Blood pressure was measured directly from the recording. Stroke volume was obtained by the planimetric integration of the area under each flow curve. Zero flow was assumed to be present at the end of diastole. Stroke work was computed as the product of mean systolic blood pressure and stroke volume. Standard statistical techniques were used to evaluate the results. All computations and plotting of data were carried out on a digital computer.[6]

[1] U. S. Catheter & Instrument Corp., Glens Falls, N. Y.
[2] Model 3400 Analog Computer, Systron-Donner Corp., Concord, Calif.
[3] Model 4568B, Hewlett-Packard Co., Palo Alto, Calif.
[4] Model 3955, Hewlett-Packard Co., Palo Alto, Calif.
[5] Model 5800, Medtronic Inc., Minneapolis, Minn.
[6] Model 1130, International Business Machines Corp., N. Y.

RESULTS

A typical recording obtained in patient C. S. is illustrated in the three panels of Fig. 1. The contour of the flow pulse is similar to those previously obtained by this technique. Note that the magnitudes of both the aortic flow and pressure pulses vary depending on the temporal relationship between the P wave and the QRS complex. This effect is more marked as the ventricular rate increases (panels B and C).

Both the stroke volume and stroke work data obtained at several selected heart rates and PR interval lengths from each patient are summarized in Table I. The stroke volume (cm^3) and the stroke work (g m) are listed as the mean and the standard error of the mean. The standard error of the mean was not calculated if there were fewer than three observations in a given group. As the directional changes for stroke work were statistically similar to those for stroke volume, only the stroke volume will be referred to in the text below. In columns three and four of Table I, a PR interval of "0" indicates that no P wave preceded the ventricular contraction. Beats without a preceding P wave serve as a base line for comparison with those beats preceded by a P wave, and hence will be considered "control" beats. For each patient, statistical comparisons were made between the stroke volumes of "control" beats at each heart rate. In columns four through nine, data obtained at the designated PR interval lengths are listed. At each heart rate for a given patient, statistical comparisons were performed to test for differences in stroke volume at different PR intervals. Only those groups having three or more observations were compared statistically. No statistical comparisons were made between data from different patients.

In eight patients data at different heart rates were available. The stroke volume of the "control" beats (column 3) decreased significantly ($P < 0.05$) as the heart rate increased, except in patient J. S. in whom the reduction in stroke volume from 17 to 15 cm^3 associated with the change in rate from 111 to 154 beats/min was not statistically significant ($P > 0.30$). For each of these eight patients, stroke volumes of "control" beats were treated as a function of heart rate, and subjected to regression analysis. For each patient, no significant difference ($P > 0.20$) could be detected at any heart rate in the stroke volume of beats preceded by a P wave with a PR interval in the range of 0.05–0.20 sec. Therefore, the stroke volumes of beats preceded by a P wave having a PR interval of 0.05–0.20 sec were combined and were subjected to a similar regression analysis. Regression lines were obtained from these computations. In one patient, A. S., the regression lines were similar, indicating that stroke volume was not altered by the presence or absence of atrial systole. For five of these

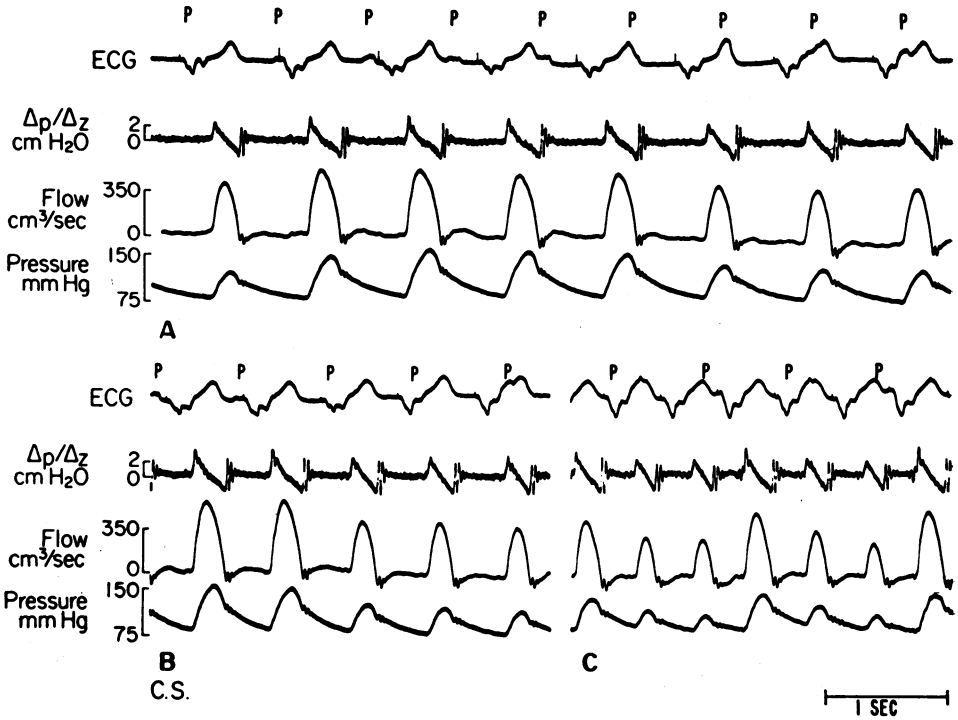

FIGURE 1 Pressure and flow recordings during ventricular pacing from patient C. S. having complete heart block. Panel A, ventricular rate 75 beats/min; panel B, ventricular rate 95 beats/min; panel C, ventricular rate 130 beats/min. ECG, pressure difference ($\Delta P/\Delta Z$), aortic blood flow, and aortic blood pressure are displayed from top down in each panel. In panel A stroke volume and blood pressure vary slightly with the differing PR intervals of beats 2, 3, 4, and 5, but both decrease markedly in the last three beats, when there was no effective atrial systole. The variations in stroke volume and blood pressure are more marked at the higher ventricular rates displayed in panels B and C.

patients, the intercepts of the regression lines were significantly different ($P < 0.05$) while the slopes were not ($P > 0.15$), i.e., the lines were parallel. In two patients, C. S. and H. D., both the intercepts and the slopes of the two regression lines were significantly different ($P < 0.05$). In patient C. S. the lines diverged slightly as the rate increased (Fig. 2) and in patient H. B. the lines converged slightly with increasing heart rates. Although the slopes were significantly different in these two patients, the actual difference in stroke volume at the slow and fast rates was quite consistent. Thus, in these seven patients, the absolute increase above "control" stroke volume for beats preceded by a P wave was essentially the same regardless of the heart rate. The magnitude of the increase in stroke volume produced by an optimally timed atrial systole was quite variable among the patients, ranging from 7 to 28 cm^3. The per cent change in stroke volume for beats preceded by a P wave, compared to "control" stroke volume at the same heart rate, was considerably greater as the heart rate increased. In Fig. 3 the change in stroke volume after a P wave divided by the "control" stroke volume for both the lowest and highest rates in each patient is given. There was a marked variation among the patients in the per cent increase in stroke volume produced by atrial systole. The increase ranged from 10 to 89% of the control at the lowest heart rate and from 41 to 145% at the highest rate. The per cent change in stroke volume rose as the rate increased.

For each patient, at a given heart rate, the stroke volumes of all beats preceded by a P wave, regardless of the PR interval, was significantly greater ($P < 0.05$) than the stroke volume of beats without a preceding P wave. Exceptions for this finding were noted in patient A. S. at all heart rates, in patient H. W. at a rate of 90 beats/min, and in patient Y. K. at PR intervals of 0.31–0.50 sec. In patient A. S. an atrial systole regardless of the PR interval failed to alter the stroke volume significantly.

As noted above, for each patient, no significant difference ($P > 0.20$) could be detected at any heart rate in the stroke volume of beats preceded by a P wave with a PR interval in the range of 0.05–0.20 sec. At a PR interval of 0.21–0.30 sec, the stroke volume in patient

H. B. at a rate of 109 beats/min was significantly less ($P < 0.05$) than at a PR interval of 0.05–0.20 sec. A similar finding was noted in patient D. L. at a rate of 95 beats/min. In patients G. S., N. T., and Y. K., a PR interval of 0.41–0.50 sec resulted in stroke volumes significantly less ($P < 0.05$) than the maximum stroke volume which occurred at the shorter PR intervals. Inspection of the data in the groups which were too small to be compared statistically corroborated the general findings described above.

DISCUSSION

The role of atrial systole in maintaining ventricular function has been of interest to circulatory physiologists for many years. Early studies in animals by Gesell (12) and Wiggers and Katz (13) documented the importance of atrial contraction in augmenting ventricular performance. More recently, experimental studies in open-chested dogs, which utilized an electromagnetic flowmeter to measure stroke volume, revealed a decrease in stroke volume ranging from 7 to 37% when atrial systole was improperly timed or absent (1, 14).

Studies of the effect of atrial contraction in man have been hampered by the inability to measure phasic flow. Using the pressure gradient technique, Snell, Luchsinger, and Shugoll (10), studied three patients with complete heart block, paced at a ventricular rate of approximately 60 beats/min. These investigators concluded that the left ventricular stroke work was maximal at PR intervals of 0.10–0.19 sec in two patients and 0.20–0.29 in the third. However, no statistical comparison of the data at the different PR intervals is given and in two of these

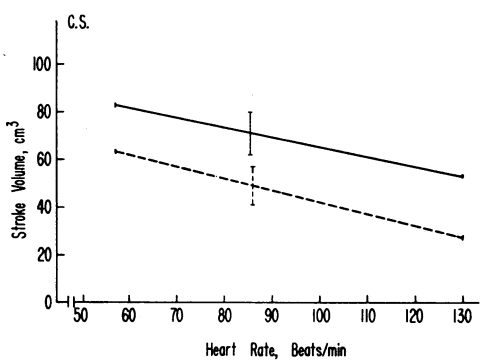

FIGURE 2 Regression lines calculated for stroke volume (on the ordinate) as a function of heart rate (on the abscissa) from patient C. S. are shown. The regression line for beats without a preceding P wave is shown as the broken line, and for beats following a P wave as the solid line. The standard error of estimate for each line is given by the crossed bar. The slopes of the lines diverge slightly as the rate increases. However, the absolute increase in stroke volume is but 3 cm^3 greater at the highest than at the lowest rate.

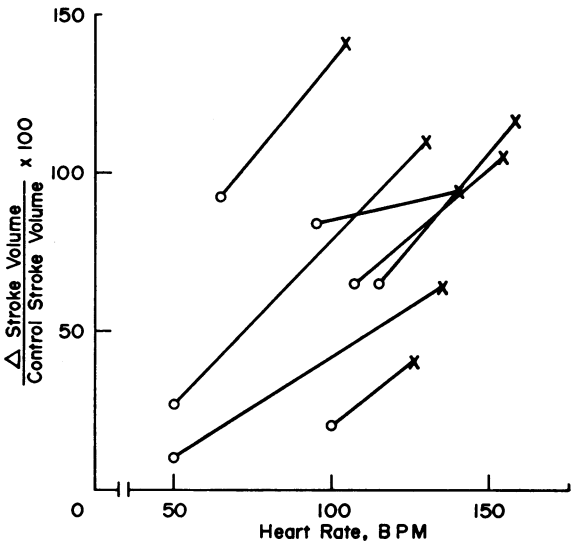

FIGURE 3 The change in stroke volume as a per cent of the control stroke volume is given for the lowest (○) and highest (X) heart rate in seven patients. The lines connect the two points from each patient. Note that there is a marked variation among patients and that the change is greater at the faster heart rates.

patients the significance of the differences in stroke work at the various PR intervals seems questionable. In two patients a PR interval of greater than 0.60 sec was associated with a marked reduction in stroke work. These values are analogous to the control data in the present study since at this PR interval atrial systole occurs during the preceding ventricular contraction. In one of these patients who was paced at a rate of 105 beats/min, a 50% reduction in left ventricular stroke work was noted when the PR interval exceeded 0.30 sec. Using the N_2O plethysmographic method for recording instantaneous pulmonary capillary blood flow, Gillespie, Greene, Karatzas, and Lee (15) found an increase in right ventricular stroke volume of 40% with a PR interval of 0.20–0.25 sec when compared to 0–0.20 and 0.40–0.90 sec in a group of patients with congenital heart block (mean heart rate 42 beats/min). In a group with acquired complete heart block (mean rate 49 beats/min) only a 13% augmentation was noted for beats with an "optimal" PR interval of 0.15–0.20 sec. Recently Benchimol (16) used a catheter-tipped Doppler ultrasonic velocity probe to estimate aortic blood velocity in several patients. He noted an increase of 15% in peak velocity of beats preceded by a P wave. In this study no mention is made of an optimal PR interval. Carleton, Passavoy, and Graettinger (17) paced the ventricle in 12 patients with heart block. These investigators used the systemic systolic blood pressure as an index of stroke volume. The per cent increase in systolic blood

TABLE 1
Effect of Atrial Systole

Patient	Heart rate	PR Interval (sec) 0 SV	0 SW	0.05–0.10 SV	0.05–0.10 SW	0.11–0.15 SV	0.11–0.15 SW
	beats/min						
H. B.	97	42 ±1	31 ±1	74 ±2	65 ±3	81 ±3	75 ±4
	109	34 ±1	28 ±2	65 ±4	58 ±5	67 ±1	62 ±2
	140	30 ±1	26 ±1	59 ±1	54 ±1	54 ±2	47 ±1
H. W.	50	79	73	87	80	93	86
	90	60 ±2	54 ±2	65 ±7	60 ±7	68	65
	109	42 ±1	39 ±1	68 ±3	65 ±3	62 ±2	60 ±2
	136	33 ±2	31 ±2	54 ±7	52 ±8	57	54
A. S.	53	68 ±2	74 ±4	68 ±3	76 ±3	65	75
	83	56 ±1	61 ±1	57 ±2	64 ±1	61 ±1	68 ±2
	111	27 ±2	29 ±2	28 ±3	32 ±4		
C. S.	57	66 ±2	55 ±2	85	74	85 ±2	74 ±3
	77	53 ±1	44 ±1	73 ±3	63 ±3	85	72
	98	36 ±1	29 ±1	62 ±3	56 ±2	67 ±2	62 ±2
	132	26 ±1	22 ±1	61 ±3	53 ±3	60 ±1	52 ±1
N. T.	69	24 ±1	23 ±1	53 ±4	52 ±5	56 ±4	58 ±9
	105	14 ±1	12 ±1	37 ±2	34 ±2	38 ±3	39 ±2
D. L.	95	50 ±1	47 ±1	63	57	70 ±2	67 ±2
	128	37 ±1	36 ±1	56 ±3	56 ±5	56 ±4	53 ±5
A. H.	118	16 ±1	17 ±1	28 ±2	32 ±2	28 ±1	30 ±2
	133	14 ±1	14 ±1	25 ±1	28 ±1	27	30
	158	10 ±1	10 ±1	25 ±1	26 ±1	25	25
J. S.	111	17 ±1	18 ±1	28 ±2	33 ±3	33 ±3	37 ±4
	154	15 ±1	14 ±1	31 ±3	31 ±2	34 ±4	31 ±2
Y. K.	65	39 ±1	51 ±1			43 ±1	56 ±1

In each column the mean and standard error for stroke volume, SV, in cubic centimeters and stroke work, SW, in gram meters is listed. If there were fewer than three observations in a group only the mean value is given.

pressure, using the least effective and optimally timed atrial systoles to estimate the atrial contribution to ventricular performance, was about 9% at rates less than 60 beats/min, approximately 19% at rates of 60–89 beats/min, and 27% at rates greater than 90 beats/min. The optimal PR interval was found to be inversely related to heart rate, and the relationship between PR interval and systolic blood pressure was parabolic.

Our findings differ somewhat from these previously reported studies in that a clearly optimal PR interval for each heart rate could not be delineated. In general, little difference was noted in stroke volumes of beats preceded by a PR interval of 0.05–0.20 sec. PR intervals of 0.41–0.50 sec were related to significantly smaller stroke volumes than those obtained at the shorter more optimal range. However, our data indicate that both stroke volume and stroke work are greater if the beat is preceded by a P wave regardless of the PR interval.

The finding that the absolute increase in left ventricular stroke volume and stroke work is essentially independent of heart rate has not previously been noted in man. Mitchell, Gupta, and Payne (1) presented a similar finding in the dog. In Table I of their report, comparing effective ventricular stroke volume for beats with and without a preceding atrial systole, the absolute change in the stroke volume after atrial systole had a mean value of 3 cm^3 at rates 60–90 beats/min and 2.9 cm^3 at 180 and 210 beats/min. The authors do not mention that the decrease in stroke volume seemed to be independent of heart rate but discuss these data in terms of the per cent change in stroke volume. However, their data support our findings that the absolute change in

PR Interval (sec)							
0.16–0.20		0.21–0.30		0.31–0.40		0.41–0.50	
SV	SW	SV	SW	SV	SW	SV	SW
80 ±1	77 ±2	76 ±2	76 ±2	68	63		
63	57	47 ±2	36 ±2				
63	58						
98	89	80	74	77 ±3	70 ±2	90	81
77	77	62 ±3	57 ±3	63 ±3	59 ±2		
61 ±1	57 ±2	49	41				
57	55						
73 ±3	81 ±4	70 ±3	76 ±3	65 ±1	70 ±2	67 ±4	74 ±6
56 ±3	64 ±3	54 ±1	60 ±1	52	59		
32	35						
91 ±1	80 ±1	87 ±3	76 ±3	83 ±2	73 ±2	82 ±2	71 ±2
77 ±4	68 ±5	73 ±3	68 ±3	72 ±3	63 ±2		
70	63	64 ±2	55 ±2				
54	56	56 ±2	57 ±3	55 ±2	55 ±3	49 ±2	47 ±2
40 ±2	38 ±1						
75	76	60 ±4	58 ±7				
				24	25		
43	50	41	47				
45	60	47 ±1	63 ±2	42 ±2	59 ±2	42 ±2	58 ±2

ventricular stroke volume produced by atrial contraction is essentially independent of heart rate. The demonstration that atrial systole may markedly augment ventricular stroke volume does not necessarily imply that the filling of the left ventricle was enhanced by a similar volume during atrial contraction. Obviously a slight change in the end-diastolic volume may enable the ventricle to empty a significantly greater volume. Accurate measurements of the amount of blood which was delivered during atrial contraction and the subsequent change in ventricular volume during ejection would be necessary to resolve this problem.

In the present study the presence of a P wave on the electrocardiogram has been equated with atrial systole. Unfortunately, we do not have recordings of either the left atrial or ventricular pressures in these patients and cannot relate these hemodynamic measurements to our data. The demonstration in one patient that atrial systole was ineffective in augmenting left ventricular stroke volume is of interest. This patient subsequently died, and at postmortem was found to have extensive fibrosis of the free wall of the left ventricle and of the interventricular septum, suggesting that left ventricular filling was limited by restrictive changes in the ventricular wall.

Our data do not shed any light as to the mechanism whereby atrial contraction enhances ventricular function. Both increased filling of the left ventricle and reduction in the amount of mitral insufficiency due to a more optimally closed mitral valve have been mentioned (2). Phonocardiograms taken on five of our patients did not demonstrate evidence of a mitral mur-

mur regardless of the PR interval. In one patient with mitral insufficiency the murmur actually was louder with the beat having a greater stroke volume. Thus, in our patients, the production of mitral insufficiency does not appear to be responsible for the lower left ventricular stroke volume in beats without a preceding P wave. This finding lends support to the opinion that mitral valve closure is not an important result of a properly timed atrial contraction (18).

The markedly increased change in stroke volume due to atrial systole for a single beat as described in our patients cannot be equated with data documenting the enhancement of cardiac output after conversion of atrial fibrillation to normal sinus rhythm. Our data provide the maximum possible change in stroke volume for a single beat whereas the change in cardiac output is controlled by the many factors which tend to regulate total flow.

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