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THE CONTRIBUTION OF ATRIAL SYSTOLE TO MITRAL DIASTOLIC BLOOD FLOW INCREASES DURING EXERCISE IN HUMANS

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SUMMARY

1. The change in the relative contribution of the early passive and later active phases of transmitral flow to left ventricular filling was studied using Doppler echocardiography in ten normal male subjects during mild exercise.

2. The peak velocity of passive flow increased during exercise by a mean of 16% whereas peak velocity of active flow increased by a mean of 89%. Hence the ratio of the peak velocities decreased in a linear fashion with a correlation coefficient of $r = -0{\cdot}95$.

3. The ratio of the Doppler-derived velocity–time integrals (equivalent to the ratio of flow) of the two phases of transmitral flow also showed a significant negative linear correlation of $r = -0{\cdot}97$.

4. Active atrial transport (atrial systole) progressively increases its contribution to overall transmitral blood flow with increasing heart rate during mild exercise. This effect is mainly mediated by an increase in flow velocity which is related to increased atrial contractility.

INTRODUCTION

The importance of atrial systole to ventricular filling was first recognized by William Harvey in 1628. Early physiologists (Gesell, 1916; Wiggers & Katz, 1921; Jochim, 1938) showed that properly timed atrial systole accounted for up to 50% of cardiac output in the isolated mammalian heart preparation. In normal man, using overdrive ventricular and atrial pacing, Benchimol, Ellis & Dimond (1965) showed that its contribution was low (perhaps about 10% of cardiac output). More recently Doppler ultrasound combined with real-time cardiac imaging (duplex scanning) has allowed transmitral flow to be studied non-invasively (Channer, Culling, Wilde & Jones, 1986; Kuo, Quinones, Rokey, Sartori, Abinader & Zoghbi, 1987).

Diastolic flow across the mitral valve occurs in two phases. In early diastole blood flows passively down the pressure gradient generated at end-systole, then in later diastole active atrial contraction causes a second flow of blood from the atrium into the ventricle prior to ventricular contraction. This dual flow gives a characteristic biphasic Doppler signal (Fig. 1). The first Doppler peak occurs immediately after the mitral valve opens (as shown by the mitral valve opening artifact) and the second Doppler peak occurs after the P wave on the simultaneous electrocardiogram showing that its timing is that of atrial systole.

If the cross-sectional area through which flow is occurring is known the volume of flow can be calculated from the velocity–time integral (Lewis, Kuo, Nelson, Limacher & Quinones, 1984). In the case of transmitral flow, if it is assumed that the mitral valve orifice changes little during the two phases of flow then a comparison of the two Doppler components of transmitral flow is an indication of the proportional

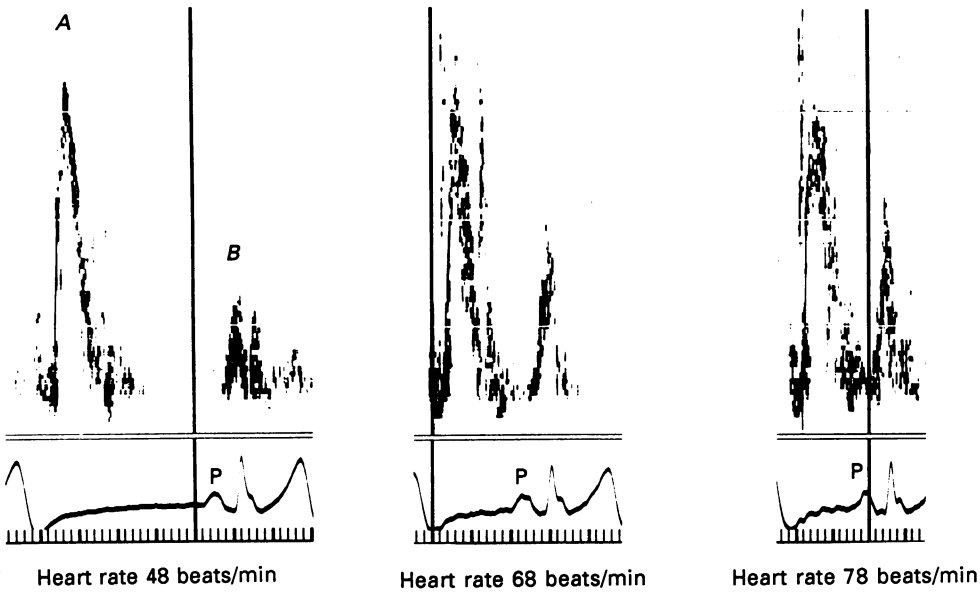

Fig. 1. Doppler flow traces at different heart rates in a single subject. Note the mitral valve opening artifact before the first peak (*A*) and the closing artifact after the second peak (*B*). The second Doppler signal follows the P wave on the electrocardiograph. Note the increase in the second peak velocity with increasing heart rate. The continuous black lines on the figures are time markers.

flow in the passive and active phases of diastole. This assumption is reasonable since it has been shown that the mitral orifice area initially decreases and then slowly increases during diastole but the maximum change is only 15% and the change from onset of passive flow to the onset of active flow is 9% (Ormiston, Shah & Wong, 1981). Moreover, since absolute measurements are not required but simply relative changes in the flow pattern, errors in imaging are not important compared with, for example, the measurement of cardiac output or valve gradients from Doppler which are inaccurate unless the peak velocity is precisely located, and the cross-sectional area measured accurately.

In this study, for the first time the contribution of atrial systole to overall transmitral flow was estimated non-invasively *in vivo* during exercise in normal individuals.

METHODS

Subjects

Ten normal male subjects of mean age 23 years (range, 21–26 years) took part in the study which was approved by the hospital Ethical Committee. Subjects gave informed verbal consent. None

had a previous history of cardiac disease, all were in sinus rhythm and none had clinical or echocardiographic evidence of mitral valve or other cardiac disease.

Methods

The experiments were performed in a cool quiet clinical laboratory. Subjects were positioned supine on a couch with a bicycle ergometer mounted on the end. Doppler recordings were made by the same observer (K.S.C.) using an Advanced Technology Laboratories mark 600 duplex scanner with a 3 MHz scan head. The apical four-chamber view was used to position the Doppler sample volume in the orifice of the mitral valve where the two cusps were seen to separate. Signals were recorded on paper of 50 mm/s during held respiration at mid-inspiration. Subjects practised breath-holding (and were instructed not to perform a Valsalva manoeuvre) before recordings were made. Subjects were asked to hold their breath at the same point of inspiration at rest and during exercise.

Flow signals were recorded at rest and during gentle bicycle exercise at intervals determined by the change in heart rate, always during held respiration. Heart rate was measured from lead II of the electrocardiogram which was simultaneously recorded on the Doppler trace. In each subject at least three recordings were made at different heart rates. Although recordings were made during held respiration, further care was taken to avoid the subject performing a Valsalva manoeuvre by limiting recording to the first few seconds of breath-holding.

Analysis of flow trace

Each spectrally analysed Doppler trace showed two peaks in diastole with heart rates up to 100 beats/min. At heart rates in excess of this the two peaks merged making their separate analysis impossible. The peak velocity of each trace was measured from the Doppler shift and expressed in cm/s (the Doppler shift is displayed in kHz and this can be converted to cm/s by multiplying by the constant 25·7). The mean of at least four (and up to ten) consecutive cardiac cycles at each heart rate was used in the analysis. The ratio of the two velocities (passive/active) was calculated. The areas under the two flow traces (velocity–time integral) were measured using computer planimetry ('Apple' digitizing tablet) in four subjects and by triangulation in six subjects. Triangulation underestimated the area compared with computer planimetry but they were significantly correlated ($r = 0{\cdot}75$, $P < 0{\cdot}01$) and the ratio of areas was consistently lower by 10%. Again at least four (and up to ten) consecutive cardiac cycles were measured at each heart rate and the mean used in the analysis.

The results were analysed using t test and linear regression. Correlation coefficients were calculated for individual subjects and then using a 'z' transformation, the mean correlation coefficient for the group was calculated.

RESULTS

Data were available for at least five subjects in each of the heart rate groups 50–59, 60–69, 70–79, 80–89, 90–99 beats/min (Tables 1 and 2).

The peak velocity of passive flow increased by 16% from a mean of 81 cm/s (range, 56–103), at mean heart rate of 53 beats/min, to 94 cm/s (79–122), at mean heart rate of 94 beats/min, and the mean values showed a significant linear correlation of $r = 0{\cdot}93$, $P < 0{\cdot}01$ (Fig. 2). The peak velocity of active flow increased by 89%, from a mean of 35 cm/s (25–49), to 66 cm/s (49–89) ($P < 0{\cdot}01$, t test), and the mean values showed a significant linear correlation of $r = 0{\cdot}99$, $P < 0{\cdot}001$ (Fig. 3). The ratio of the two velocities showed significant negative linear correlations with increasing heart rate (Fig. 4) and the group mean correlation coefficient produced by 'z' transformation was $r = -0{\cdot}95$, $P < 0{\cdot}01$, illustrating that with increasing heart rate the relative change in diastolic blood flow velocity is greater during atrial systole. Similarly the ratio of the two areas showed significant negative linear correlations with increasing heart rate (Fig. 5) and the group mean correlation coefficient

TABLE 1. Velocity ratios (VR) for the subjects in each of the heart rate (HR) groups

Heart rate (beats/min):	50–59	60–69	70–79	80–89	90–99	$r(-)$
D.K.	3·20	2·23	1·86	1·70	—	0·88
E.S.	1·60	1·39	1·23	1·12	—	0·98
P.W.	2·10	2·79	—	1·95	—	0·25
B.H.	2·38	—	1·73	1·51	—	0·99
J.H.	—	—	2·36	1·80	1·53	0·97
S.K.	2·76	2·42	1·91	1·70	1·44	0·99
P.M.	—	—	1·38	1·27	1·02	0·98
J.S.	—	2·00	2·03	1·80	1·56	0·94
S.R.	—	1·64	1·65	1·59	1·65	0·06
J.P.	—	1·78	1·45	1·38	—	0·96
Mean VR	2·41	2·04	1·80	1·58	1·44	0·95*
Mean HR	53	64	74	83	94	—

* Group correlation coefficient produced by 'z' transformation of individual correlation coefficients.

TABLE 2. Mitral valve flow ratio (MVFR = passive/active flow) for the subjects in each of the heart rate (HR) groups

Heart rate (beats/min):	50–59	60–69	70–79	80–89	90–99	$r(-)$
D.K.	3·91	4·18	2·71	2·51	—	0·91
E.S.	2·69	2·27	2·29	1·80	—	0·97
P.W.	3·73	3·25	—	2·28	—	0·99
B.H.	3·92	—	2·34	2·21	—	0·97
J.H.	—	—	3·45	2·43	1·82	0·97
S.K.	6·35	4·69	4·26	2·99	2·60	0·95
P.M.	—	—	2·24	2·07	1·80	0·99
J.S.	—	3·15	3·22	2·73	—	0·75
S.R.	—	3·95	3·66	3·14	2·54	0·99
J.P.	—	3·71	2·79	2·50	—	0·97
Mean MVFR	4·12	3·60	3·00	2·47	2·19	0·97*
Mean HR	53	64	74	83	94	—

* Group correlation coefficient produced by 'z' transformation of individual correlation coefficients.

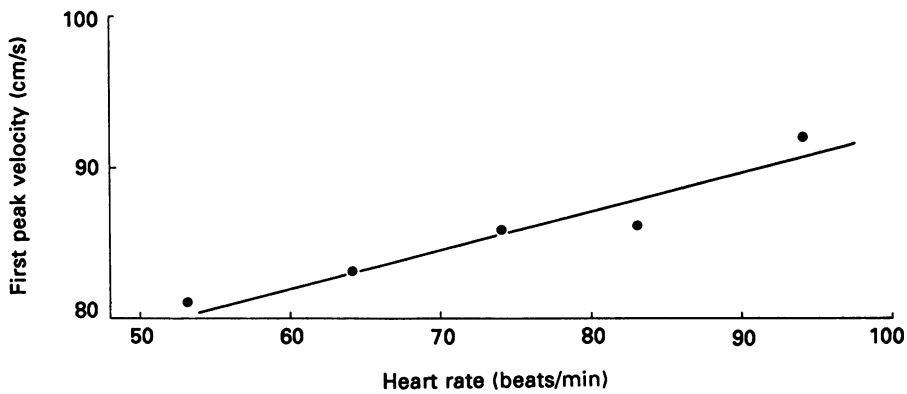

Fig. 2. Change in mean first peak velocity (passive flow) with increasing heart rate during exercise ($r = 0·93$).

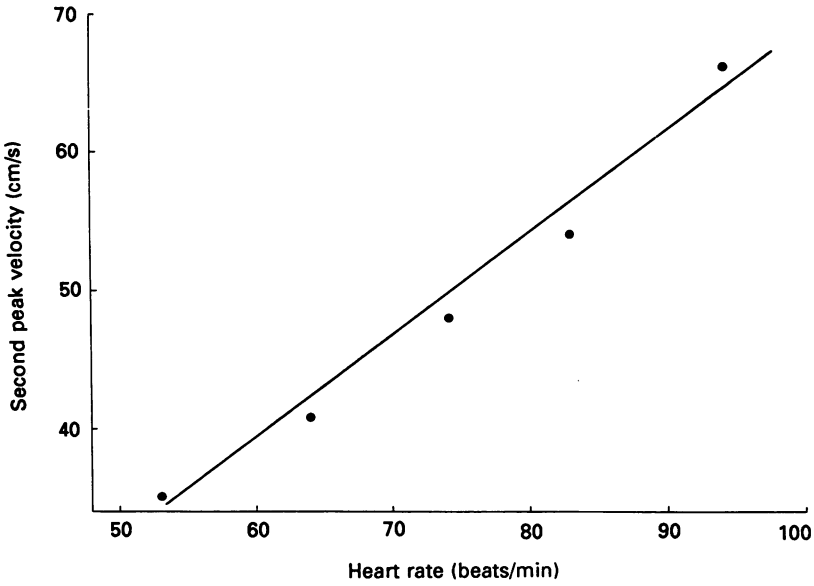

Fig. 3. Change in mean second peak velocity (active flow) with increasing heart rate during exercise ($r = 0{\cdot}99$).

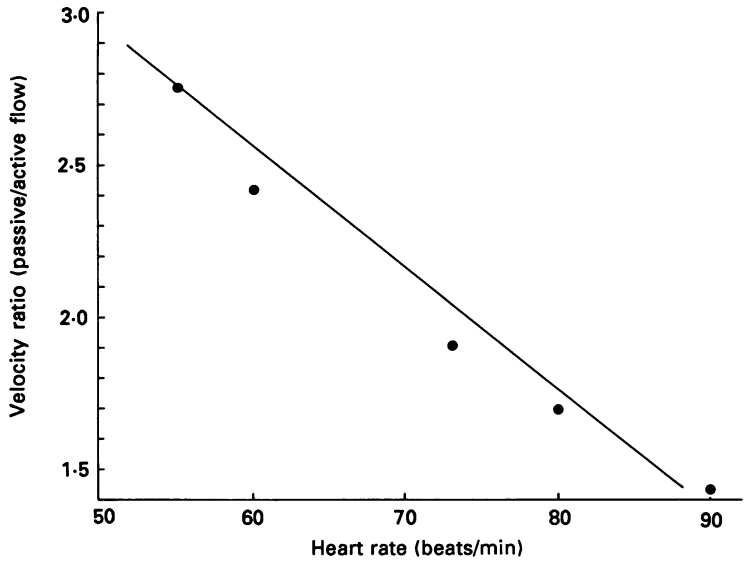

Fig. 4. Change in velocity ratio with increasing heart rate during exercise in subject S.K. ($r = -0{\cdot}99$).

was $r = -0{\cdot}97$, $P < 0{\cdot}001$, illustrating that with the increasing heart rate caused by exercise the proportion of diastolic blood flow occurring in atrial systole increases.

DISCUSSION

The contribution of atrial systole to ventricular filling has been extensively investigated by early physiologists using isolated mammalian heart preparations and found to account for up to 50% of cardiac output. The concept that the ventricle

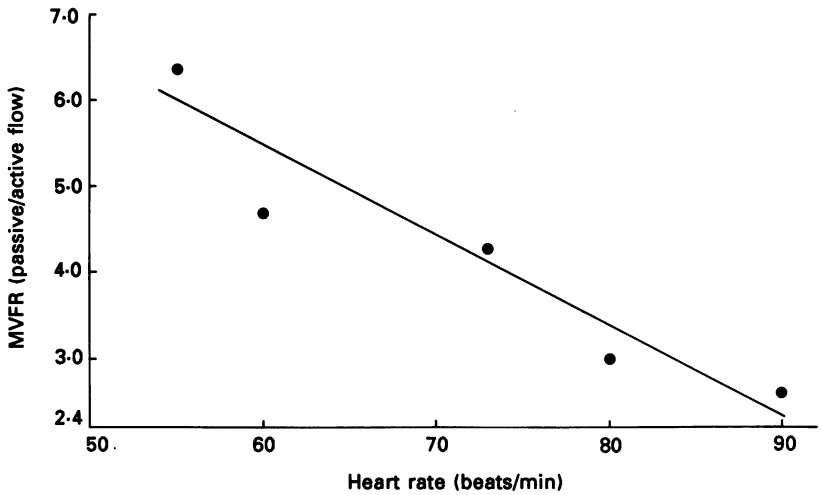

Fig. 5. Change in mitral valve flow ratio (MVFR) with increasing heart rate during exercise in subject S.K. ($r = -0{\cdot}95$).

plays a part in its own filling by exerting a pulling force during ventricular relaxation has long been debated, but dismissed, by Harvey (1628) and most contemporary physiologists (see Channer & Jones, 1988, for historical review). In man the role of atrial systole in ventricular filling has previously been measured invasively from changes seen on cineangiograms (Matsuda, Toma, Ogawa, Matsuzaki, Katayama, Fujii, Yoshino, Moritani, Kumada & Kusukawa, 1983) and by using pacing techniques to separate the effect of ventricular contraction alone from that of atrioventricular synchronous contraction (Benchimol *et al.* 1965). With the advent of Doppler echocardiography an estimation of the contribution to ventricular filling of atrial systole can be made non-invasively and under changing physiological conditions. The two Doppler peaks correspond to the early passive flow (with onset immediately after the mitral valve opens) and later active flow which follows atrial contraction (as judged by the timing of the P wave on the simultaneous electrocardiograph) (Fig. 1).

The calculation of volume flow from the velocity–time integral relies on knowledge of the cross-sectional area through which flow is occurring (Lewis *et al.* 1984). By the use of a ratio in this study we have avoided the need to calculate mitral valve area and volume flow and thus have eliminated a potential major source of error since we have not calculated absolute values of flow. The validity of the use of a ratio relies

upon the assumption that mitral valve area does not change significantly in the two phases of diastole. Although mitral valve leaflet excursion changes during diastole and is responsible for the characteristic M-shaped appearance of M-mode tracings, this may not reflect changes in the mitral orifice. Available data suggest that mitral orifice area initially decreases then increases during diastole but the overall change is small, about 9% (Ormiston *et al.* 1981). An increase in mitral orifice area would actually decrease flow velocity and since we observed a relative increase in atrial systolic velocity compared with passive flow velocity, this cannot be accounted for by the change in the orifice area. Indeed, at faster heart rates with shorter diastolic periods the two flows are temporally close together making any significant change in orifice area between the two phases of diastolic flow very unlikely.

In normal man atrial systole does not contribute more than about 10% to cardiac output (Benchimol *et al.* 1965) and the high resting mitral valve flow ratio found in our normal subjects would confirm this. However, in this study we have shown that the second phase of diastolic flow following atrial systole increases more than that of the first flow with exercise, thus increasing its overall contribution to ventricular filling. The increase is predominantly seen as a proportionately greater increase in flow velocity. Previous physiological studies on isolated mammalian hearts have shown that the atria respond in the same way as the ventricles to stretch (Gesell, 1916; Wiggers & Katz, 1921) and to autonomic influences (Gesell, 1916; Wiggers & Katz, 1921; Sarnoff, Brockman, Gilmore, Linden & Mitchell, 1960). Vagal stimulation decreases and sympathetic stimulation increases atrial contractility. Thus, we believe that the changes we have demonstrated in the latter diastolic flow which we believe are caused by atrial systole would be predicted from the known physiological adaptations of exercise. During exercise, left atrial volume would be expected to increase consequent upon the increase in venous return to the heart. This would cause an increase in atrial contractility by Starling's law. However, an exercise-induced increase in heart rate with a subsequent shortening of the diastolic period would tend to decrease left atrial volume and offset this change. Increased sympathetic drive during exercise would further augment atrial contractility.

Although atrial systole may have only a minor supportive role in normal cardiac physiology its importance in maintaining cardiac output becomes apparent when the left ventricle is damaged. It has been estimated that atrial systole may contribute up to 50% of cardiac output under these circumstances (Rahimtoola, Ehsani, Sinno, Loeb, Rosen & Gunnar, 1975; DeMaria, Miller, Amsterdam, Markson & Mason, 1976), but this is dependent on ventricular filling pressure; when filling pressure is high the contribution of atrial systole is lower (Greenberg, Chatterjee, Parmley, Werner & Holly, 1979; Channer *et al.* 1986). Our study would suggest that the importance of atrial systole to overall cardiac output in impaired ventricles without high filling pressure would increase further on exercise. This has indeed been shown in patients with heart block who have been paced either by ventricular stimulation alone and thus have atrioventricular asynchrony or with atrioventricular synchronous pacing (Pehrsson & Astrom, 1983; Ausubel, Steingart, Shimshi, Klementowicz & Furman, 1985).

In conclusion, this study shows that the Doppler pattern of transmitral flow changes during exercise. There is a proportionately greater increase in the velocity

of flow of the second diastolic peak. This second diastolic flow corresponds with the onset of atrial contraction as judged by the P wave on the electrocardiograph. Thus, we conclude that atrial systole progressively contributes more to diastolic ventricular filling with increasing heart rates during exercise, and that this effect is mediated predominantly by increased velocity of flow itself probably secondary to increased atrial contractility.

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