Eur J Echocardiography (2003) **4,** 286–291
doi:10.1016/S1525-2167(03)00008-8

Left Ventricular Mechanics During Exercise: A Doppler and Tissue Doppler Study

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Aims: To study left ventricular mechanics of exercise with Doppler and tissue Doppler.

Methods and Results: Twenty-one males (mean age, 26; height, 184 cm; weight, 84 kg), exercised on a bicycle, with increasing workload, with oxygen uptake, Doppler flow and tissue Doppler recordings during exercise. There was correlation between peak systolic LVOT flow and annulus velocity; $R = 0.72$, ($p < 0.001$) and between peak mitral E flow and annulus E_a velocity; $R = 0.68$ ($p < 0.001$). Finally there was correlation between peak LVOT and mitral flow velocity; $R = 0.83$ ($p < 0.001$) and peak systolic and early diastolic annulus velocity $R = 0.69$ ($p < 0.001$). All intervals of the heart cycle decreased with RR-interval. There was a linear relation between diastolic filling and RR-interval, while ejection period was less increased with RR-intervals above 600 ms, and thus not a linear relationship. There was no change in E/E_a ratio during exercise.

Conclusions: Mechanism for increased filling as well as ejection during exercise seems to be increased contraction and relaxation velocity, with no evidence of Frank–Starling mechanism. Bazett's formula gives a better heart rate correction of LVET at high heart rates than Weissler's.

(Eur J Echocardiography 2003; 4: 286–291)

Key Words: exercise echo; Doppler echocardiography; tissue Doppler; time intervals.

Background

During incremental exercise, there is evidence for increased stroke volume up to maximal oxygen uptake, in endurance trained athletes[1–4]. This leads to decreased duration of time intervals of the heart cycle. At low heart rates, the RR-interval shortens mainly by shortening of the diastasis, with less shortening of ejection and filling periods. When diastasis is reduced to zero, the early filling (E) and late (atrial-A) wave fuses, at HR of about 120[5]. Further shortening of the RR-interval necessitates shortening of ejection and filling periods, and hence, higher flow rates to maintain or increase stroke volume.

There is evidence of a shortening of ejection time (LVET) with increasing heart rate, linear as proposed by Weissler *et al.*[6]: $\mathrm{LVET_c} = \mathrm{LVET} + 1.7 \times \mathrm{HR}$, or non-linear as proposed by Bazett[7] for QT-interval: $\mathrm{QT_c} = \mathrm{QT}/\sqrt{\mathrm{RR}}$. (The which may apply although LVET is shorter than the QT-interval.) Increased ejection flow rate at low and high intensity exercise, are shown by radionuclide technique[8] and Doppler echocardiography[9]. Peak ejection flow velocity is related to contractility and to flow rate in the absence of obstruction, increased contractility during exercise is shown by EF studies[10,11]. A direct method for measuring contractility is Doppler tissue imaging, especially peak systolic mitral annulus velocity[12,13].

In diastole there is evidence of a linear relation between diastolic filling period (DFP) and RR-interval even at low heart rates[14], necessitating a compensatory increased filling rate, which is documented by radionuclide[8,15] and Doppler[5,16] techniques. The role of the Frank–Starling mechanism with increased flow due to increased filling pressure versus left ventricular 'suction' due to catecholamine-induced increased relaxation rate remains unclear. Relaxation rate increases by catecholamines[17], and invasive studies indicate decreased ventricular filling pressure during exercise[18]. Non-invasive studies have indicated

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Received 16 October 2002; revised manuscript received 20 January 2003; accepted 23 January 2003.

1525-2167/03/ $30.00/0

a role for the Frank–Starling mechanism[8], mainly in the elderly[19].

A direct measure of diastolic function is the relaxation velocity by tissue Doppler, especially peak annulus velocity during early filling[20]. A recent study[21] has shown increased annulus velocity during exercise. Early mitral annulus velocity is less load-dependent than mitral flow velocity, and the ratio between them, E/E_a, is related to filling pressure[22,23].

A combined myocardial performance index (MPI) of left ventricular systolic and diastolic function based on time intervals (MPI = Isovolumic contraction + isovolumic relaxation/LVET ejection time) has been proposed[24].

The aim of this study was to

Determine contraction and relaxation rates by tissue Doppler and compare with flow velocities for evaluation of the mechanisms for increased cardiac performance.

Determine possible changes in left ventricular filling pressure and the importance of the Frank–Starling effect.

Determine time intervals of the heart cycle, and their relation to HR and flow velocities.

Material and Methods

Subjects

Twenty-one healthy male volunteers participated; mean age 26 years (19–41), height 184 cm (174–195), weight 84 kg (67–109). Training background was varied (0–15 h/week, average 4.6), reflecting a normal young male population. None were obese, and all had normal resting echocardiography. Written consent was obtained. The study was approved by the regional ethical committee for medical research.

Exercise Protocol

Exercise was performed sitting on an electronically braked ergometer bicycle. Oxygen uptake (VO_2) was measured continuously, for determining sub maximal and peak aerobic exercise capacity.

Stage 0 was resting on the bicycle. Exercise started at 50 W for warming up, and then workload intervals were HR-dependent, work was stabilised with a constant workload at predetermined heart rates of 100 (stage 1), 120 (stage 2), 150 (stage 3), for echocardiographic recordings. After stage 3, workload was increased to reach peak VO_2. Echocardiography was also attempted during this stage of increasing work (stage 4), but before peak oxygen uptake was reached.

Some subjects had HR of 100 at stage 0, and some had a rapid increase of HR to 120 or 150 at low workloads. Above HR 150, echocardiography became difficult due to exaggerated motion of the upper body, reducing the yield of data at this stage. Thus not all subjects were examined at all stages. Exercise protocol as well as the number of subjects examined at each stage are summarised in Table 1, showing stage 2 to be about 40% of peak VO_2, and stage 4 to be 90%.

Echocardiography

All recordings were done with a Vingmed Vivid Five scanner (GE Vingmed Ultrasound, Horten, Norway). Subjects were examined at rest, both in the left lateral supine position, and upright on the bicycle before exercise (stage 0) and at stages 1–4 in the exercise protocol. Apical four- and two-chamber views were acquired in the colour tissue Doppler mode, with frame rate of 110–130. PRF was 1.5 KHz to avoid aliasing in diastole. Pulsed Doppler flow recordings of left ventricular outflow and mitral inflow was obtained from the apical view. All recordings were transferred to a computer for off-line analysis in echoPAC (GE Vingmed Ultrasound, Horten, Norway).

Mitral annulus velocity in systole and early and late diastole was measured by colour tissue Doppler in the septal and lateral points in the four-chamber plane and the anterior and posterior points in the two-chamber plane and averaged. From Doppler flow recordings, peak systolic ejection velocity, peak mitral inflow velocity in early and late diastole, ejection time and corrected ejection time by Weissler's and Bazett's formulae, diastolic filling period, and isovolumic relaxation time was measured. Total isovolumic time was calculated as RR-interval − (ejection + filling time). Ratio of peak early diastolic flow versus annulus velocity ratio (E/E_a)[22,23] and MPI[24] was calculated.

Statistics

Tests for differences between stages are by two-tailed unpaired Student's *t*-test. A *p* value below 0.05 was considered statistically significant. Correlations are by Pearson's R, *p* values are two-tailed.

Table 1. Exercise stages.

Stage		0	1	2	3	4	$VO_{2\,peak}$
Number of subjects (echo)		21	12	18	20	13	0
HR	Average	76	104	127	159	184	192
	SD	13.6	6.7	4.5	7.2	7.5	7.4
Workload (W)	Average	0	98	116	200	302	338
	SD	–	4.1	28.6	49.5	82.9	74.2
VO_2 (ml/kg/min)	Average	6.2	21.6	23.9	35.8	48.8	55.4
	SD	0.9	2.7	6.8	8.4	10.7	9.5

Results

Velocities

Systolic and early and late diastolic peak velocities of flow and annulus motion decreased from supine to sitting, while heart rate increased. Average measurements and calculations are given in Table 2. During exercise all increased gradually. There was significant correlation between peak systolic flow velocity and peak systolic annulus velocity; R = 0.72, (95% CI: 0.62–0.80 $p < 0.001$) and between peak mitral flow velocity and peak diastolic annulus velocity; R = 0.68 (0.57–0.77, $p < 0.001$). Finally there was correlation between peak LVOT velocity and mitral flow velocity; R = 0.83 (0.77–0.88, $p < 0.001$) and peak systolic and diastolic annulus velocity; R = 0.69 (0.57–0.78, $p < 0.001$). Thus there was little change in E/E_a, although statistical significance is reached at stage 0. Correlation between VO_2—both absolute and relative to body mass—and all flow and tissue velocities, respectively, ranged from 0.75 to 0.81, with no significant differences between the different variables. Flow and tissue velocities of the A-wave decreased from supine to sitting, and increased again to stage 1. Above stage 1 there was E and A fusion both in tissue and flow.

Intervals

All intervals of the heart cycle decreased gradually as heart rate increased (Fig. 1). At HR 120 there was E/A fusion, and hence diastasis was reduced to zero. There was measurable isovolumic relaxation interval at all heart rates, with total isovolumic time longer than IVR. At rest, diastolic filling period was longer than ejection time, and shortened most at the first stage of exercise. After the first stage, they were similar, shortening at the same rate. As RR-interval and diastolic filling decreased in parallel (Fig. 1a), there was a close linear relation between RR-interval and diastolic filling (R = 0.97, 95% CI: 0.95–0.98, $p < 0.001$) (Fig. 1b). Ejection time and total isovolumic time increased less with RR-interval > 600; R = 0.89 (0.83–0.92) and 0.61 (0.51–0.74), respectively.

Bazett's formula gives a corrected ejection period of 288 ms (±2 SD: 225–352) and Weissler's 417 ms (±2 SD: 349–485). The correction is more linear with Bazett's, while Weissler's correction results in increase with HR > 100. This is summarised in Fig. 2.

MPI decreased from 0.47 to 0.24 during exercise (Fig. 2c) ($p < 0.01$ from rest to peak), but the change reached significance only at the last stage.

Discussion

Velocities

The present study shows a gradual increase in the filling and ejection velocities, with close relation between flow and tissue velocities as well as between peak velocities in systole and diastole. The relation between flow and tissue velocities is a strong indication that the mechanism for flow velocity increase is increased in contractility and relaxation rate. In addition the correlation between systolic and diastolic velocities, indicates that both contractility and relaxation rate are increased by the increased sympathetic tone of exercise, which is in accordance

Table 2. Main echocardiographic findings at each stage.

Stage	Supine	0	1	2	3	4
HR (per min)	65	76*	104*	127*	159*	184*
S (cm/s)	113 (19)	96* (16.7)	132* (17)	155* (21)	165* (16)	167† (19)
E (cm/s)	93 (23)	74* (14)	98* (34)	108† (16)	144* (19)	152† (19)
A (cm/s)	64 (58)	49 (14)	81* (30)	–	–	–
S_a (cm/s)	8.5 (1.7)	8.2 (1.5)	10.4* (1.4)	12.5* (2.3)	15.2* (2.7)	16.3† (2.7)
E_a (cm/s)	12.7 (1.8)	8.0* (2.0)	11.3* (1.9)	12.7† (2.5)	16.4* (2.1)	18.4† (3.7)
E/E_a	7.4 (1.5)	9.7* (2.9)	9.6 (1.4)	8.8 (2.1)	8.8 (1.7)	8.4 (2.4)
A_a (cm/s)	6.7 (1.7)	4.7* (1.7)	8.5* (2.3)	–	–	–
RR (ms)	959 (182)	821* (161)	576* (40)	473* (17)	377* (17)	326* (12)
LVET (ms)	287 (22)	255* (32)	235* (21)	208* (25)	166* (21)	157† (21)
LVETc (W)	397 (17)	383* (25)	412* (20)	423† (21)	436† (26)	470* (22)
LVETc (B)	296 (20)	283 (27)	309* (26)	302† (34)	270* (36)	274† (35)
DFP (ms)	537 (133)	446* (144)	242* (93)	199* (34)	156* (16)	134* (15)
IVR (ms)	71 (15)	74 (16)	46* (17)	41† (16)	33† (15)	32† (15)
IV_t (ms)	134 (67)	121 (85)	102† (81)	67† (44)	57† (27)	35* (26)
MPI	0.46 (0.22)	0.49 (0.35)	0.38 (0.23)	0.34 (0.25)	0.37 (0.22)	0.24 (0.19)

Standard deviation for each stage in parentheses. * denote statistically significant change from previous stage ($p < 0.05$), † denote statistically significant change from second previous stage. S, peak LVOT ejection velocity; E, peak mitral flow velocity during early filling; A, peak mitral flow during atrial systole; S_a, peak mitral annulus velocity during systole by tissue Doppler; E_a, peak annulus velocity during early filling; A_a, peak annulus velocity during atrial systole; RR, RR-interval; LVET, left ventricular ejection time; LVETc, HR corrected ejection time by Weissler (W) and Bazett's (B) formulae, respectively; DFP, diastolic filling period; IVR, isovolumic relaxation time; IV_t, total isovolumic time; and MPI, myocardial performance index.

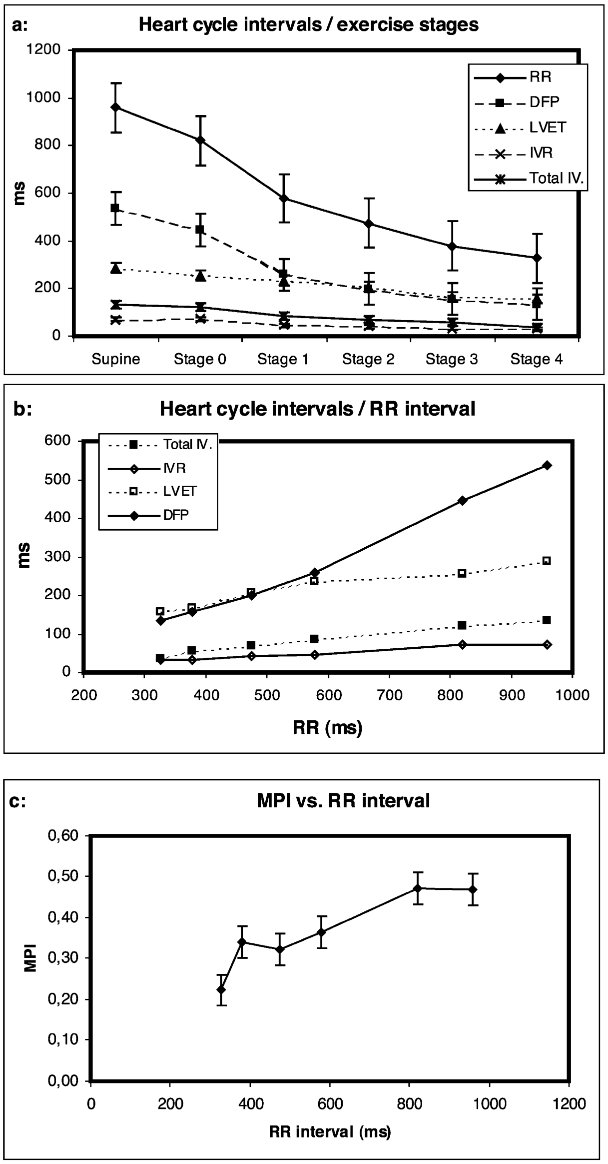

Figure 1. Heart cycle intervals. (a) At each exercise stage and (b) related to RR-interval. The linear relation between DFP and RR-interval is evident. Up to HR > 100, RR-interval and DFP shortens mainly by shortening diastasis, between HR 100 and 120 there is E and A fusion due to no diastasis and nearly parallel shortening of all intervals. (c) MPI. This is significantly lower at the lowest RR-interval, but apart from this, there is no significant change with HR, although this may be due to low precision of measurements as there is a visible trend.

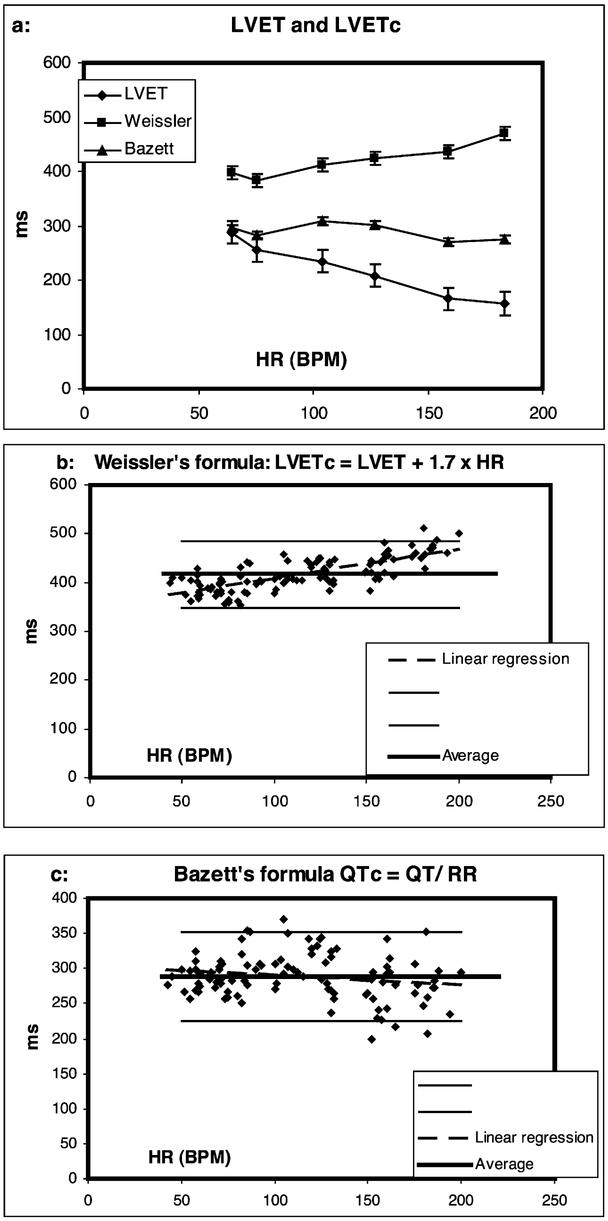

Figure 2. (a) Average ejection time for each heart rate. LVET is shown to fall with increasing heart rate. Corrected LVET with Weissler's formula tend to increase with heart rate, while Bazett's formula shows no significant change from low to high HR. Both corrections show a small dip in LVET at stage 1. (b) LVET by Weissler's correction plotted against heart rate for each individual measurement. In this study average LVET is 417 ms, with 95% population interval of 349–485 ms, indicated on the figure. Linear regression, however, shows corrected LVET to increase with increasing HR. (c) Correction by Bazett's formula. This gives lower absolute values, with an average of 288 ms, and an interval of 225–352. Linear regression shows a small decrease with increasing HR, which is not significant. The normal value for QT_c of 400 ms is longer, as QT is longer than LVET.

with previous findings[17,18]. Nonogi *et al.*[18] also found that lowest filling pressure (during early filling), decreased with exercise, while mean filling pressure was unchanged. The findings with tissue Doppler are in accordance with D'Andrea *et al.*[21]. D'Andrea takes this as an indication of the Frank–Starling mechanism at work, disregarding that tissue Doppler measurements are relatively load-independent[22,23]. Thus, myocardial relaxation and contractility are interdependent, both relate to the myocardial performance in exercise, shown by the relation to VO_2. Velocities during atrial systole are also shown to increase during exercise[26], and there is agreement between the present study from stage 0 to 1 and that of Channer and Jones, which have not been exercised above HR 100. The increase in A-wave velocity may be due to increased atrial contractility, but also partly due to the summation of early and late velocities once diastasis is shorter than deceleration time of the E-wave. Once there is E and A fusion, Doppler cannot distinguish the relative importance of relaxation and atrial contractility, and the peak velocity is the sum of both. Thus, the peak early diastolic velocity below HR 100 shows the increase in relaxation rate, and above 100 the sum of relaxation and atrial contractility, the relative importance of the two factors cannot be distinguished (Fig. 3).

Filling Pressure

The constant E/E_a indicates a constant filling pressure, and thus no indication of Frank–Starling mechanism. E/E_a ratio is slightly higher than in previous studies[9,10], as tissue velocity is by colour Doppler[25]. The lack of evidence of the Frank–Starling effect in this group of young males is in accordance with Gerstenblith *et al.*[19]. Increased filling velocity without increased filling pressure is a case for left ventricular 'suction', in accordance with invasive studies[17].

Position

The change from supine to sitting position demonstrated reduced ventricular filling as shown by the reduced mitral flow velocities, consistent with decreased venous return. Corresponding to a similar reduction in stroke volume, there is reduced flow velocity, and an increased HR. However, E/E_a ratio increases slightly but significantly ($p<0.003$), pressure. The increase is small, and the meaning uncertain. Contractility as shown by systolic annulus velocity, remained unchanged, consistent with lower stroke volume balanced by shorter ejection time.

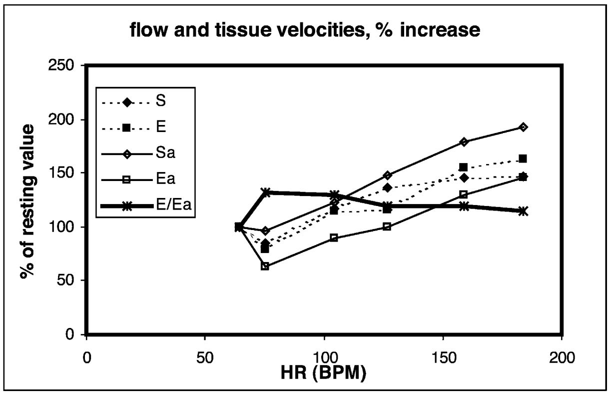

Figure 3. Flow and tissue velocities, per cent increase for equal scaling. During exercise there is parallel increase in both systolic and diastolic, and both flow and tissue velocities, as shown by the correlations (see text). From supine to sitting there is a decrease in flow velocities, but not in systolic annular velocity, as there is an increase in HR. There is little increase in E/E ratio, during exercise, although a small increase from supine to sitting rest ($p<0.05$) can be observed.

Intervals

All intervals of the heart cycle shortens relative to increasing heart rate, but below 100, RR-interval and DFP shortens mainly by reduction of diastasis. Above 100, diastasis is zero, with fusion of the E and A waves, and hence all intervals shorten in parallel. Thus, the ejection period curve has a non-linear relation with RR-interval, with a break at RR-interval of 600. The finding that Bazett's formula corrects LVET better than Weissler's is simply due to this non-linearity. In resting echocardiography with HR < 100, Weissler's correction functions well enough, and may even be more correct.

The MPI shortens during exercise (Fig. 1c), but the trend does not reach significance before the last stage. This is probably due to the variability of measurements, demonstrating the limitation of the index.

Limitations

A major limitation is that measurements are not blinded. However, as stages were defined by heart rate, blinded analysis was not possible due to the heart rate being clearly apparent in the recordings.

The study group consists entirely of young, fit males. The findings in similar studies may be influenced by both levels of training[2,3], gender[4,27,28] and age[19,27,28].

Data are consecutive, not independent, and reflects only intra-individual changes.

Echocardiography is difficult in the sitting position, increasingly so with increasing workload. This may lead to misalignment with angle deviation and underestimation of velocities. In tissue Doppler, this is reduced, points by averaging four points. On the other hand, frame rate (sampling frequency) may be too low to measure peak velocities at high HR. Doppler flow measurements suffer from underestimation by misalignment with peak velocity as well. Thus increasing underestimation of peak velocities with increasing workload may be assumed. Time intervals will not be similarly affected. A final concern is the number of dropouts. At stage 1, this was due to higher heart rates at initial exercise, but here the average falls on the trend line. At stage 4, i.e. above HR 150, however, with a 35% dropout rate, results should be interpreted by caution.

Conclusions

There is a gradual and parallel increase in contraction and relaxation rates by tissue Doppler with increasing workload in graded exercise. This correlates to peak flow velocities by Doppler flow, and to VO_2. There is no indication of increased filling pressure, so the Frank–Starling mechanism cannot be demonstrated. The findings support the hypothesis that the main mechanism for increased filling velocity is increased relaxation velocity (i.e. left ventricular ‘suction’), and increased atrial contractility, and the mechanism for increased stroke volume is increased LV contractility, presumably regulated by sympathetic tone found.

Diastolic filling period is linearly related to RR-interval. Ejection time is closely related to diastolic filling above HR 100. Bazett’s formula gives a better heart rate correction of LVET at high heart rates than Weissler’s.

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