Assessment of the longitudinal and circumferential left ventricular function at rest and during exercise in healthy elderly individuals by tissue-Doppler echocardiography: relationship with heart rate

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ABSTRACT

Tissue-Doppler echocardiography (TDE) has been introduced to quantify stress echocardiography by means of assessing the left ventricular (LV) segmental myocardial velocities and excursion. The interaction between LV long- and short-axis function during physical exercise has not been elucidated completely. The aim of the present study was to investigate long- and short-axis LV function, as assessed by myocardial velocities and excursions at rest and during exercise and its possible relationship with heart rate in healthy elderly individuals by TDE. Twenty-seven individuals underwent an exercise test in the supine position on a bicycle ergometer. The initial workload was 30 Watts, followed by 20-Watt increments every third minute. Standard echocardiographic images with super-imposed colour TDE were digitized at the end of each step. The following variables were studied in the LV long- and short-axis: myocardial peak systolic velocity (PSV) and excursion, isovolumic contraction and relaxation times, peak velocity at early diastole (E′-wave) and peak velocity at late diastole (A′-wave) and the E′/A′ ratio. Increments in myocardial peak systolic velocity and excursion in the LV long-axis were more pronounced during low workloads. The increase in those variables in the short-axis occurred mainly at higher exercise loads. The improvement in LV long- and short-axis functions was closely related to the increase in the heart rate. Shortening of the isovolumic contraction and relaxation times occurred only at the initial stages of exercise. An increase in the long-axis E′/A′ ratio occurred during exercise, whereas this ratio was unchanged in the short-axis. In conclusion, during exercise, the LV long- and short-axis functions behave differently, and increases in LV long- and short-axis functions are related to changes in heart rate. Therefore, in the interpretation of echocardiographic findings during exercise stress echocardiography, these facts have to be taken into account.

INTRODUCTION

Quantitative stress echocardiography using tissue-Doppler echocardiography (TDE) is possibly a useful tool to detect wall motion abnormalities secondary to coronary artery disease [1,2]. The rationale for the use of TDE lies behind the close relationship between the TDE-derived myocardial velocities and both the

Key words: exercise, left ventricular function, tissue Doppler echocardiography.

Abbreviations: A′-wave, peak velocity at late diastole; E′-wave, peak velocity at early diastole; IVCT, isovolumic contraction time; IVRT, isovolumic relaxation time; LV, left ventricular; PSV, peak systolic velocity; TDE, tissue-Doppler echocardiography.

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myocardial structure and β-adrenergic receptor density in heart muscle [3]. In addition, TDE has been shown to be an accurate method for detecting and quantifying anomalies in myocardial velocities induced by acute ischaemia and reperfusion [4,5]. Although the feasibility of TDE for the diagnosis of coronary artery disease has been based on the assessment of the longitudinal velocities of the left ventricular (LV) walls during dobutamine stress echocardiography [1,2], assessment of both circumferential and longitudinal LV function is often necessary [6]. Although TDE-derived myocardial velocities are presumably a surrogate marker for myocardial β-receptor function [3], it remains to be determined if direct β-adrenergic stimulation by dobutamine and by exercise alter the TDE-derived variables in a similar fashion. Since the pharmacological effects of dobutamine may not be totally blocked by cholinergic stimulation by atropine [7], it is physiologically plausible that other factors, such as volume status, body positions and modality of stress, are important factors that might influence TDE variables. Human studies of the contraction behaviour of the circumferential fibres during exercise are relatively scarce, although human and animal data suggest that ischaemia induced by coronary artery occlusion alters the velocity gradient of the myocardial circumferential excursion [8,9]. Therefore it is necessary to investigate whether exercise results in a similar TDE response both circumferentially as well as longitudinally and to assess their dependence on chronotropic behaviour. In the present study, we have measured the LV short- as well as long-axis velocities and their integrals (excursion) at rest and during supine bicycle exercise in a group of healthy elderly human subjects comparable in age with those usually referred for stress echocardiography.

METHODS

Population
A group of 27 healthy elderly individuals was studied. The mean age was 69 (range, 60–87) years and the group consisted of 11 men (41 %) and 16 women (59 %). The individuals were recruited by advertising in 15 different local senior organizations newsletters. None of them had cardiovascular symptoms, were on treatment with cardiovascular pharmacological agents and all of them performed an exercise ECG test during which none had clinical symptoms or electrocardiographic signs of exercise-induced myocardial ischemia. The Ethical Committee at Huddinge University Hospital approved the study. All individuals received written information about the study and gave informed consent.

Exercise test protocol
For the purposes of stress echocardiography, all individuals underwent a bicycle exercise test. The subjects performed the stress test in supine left lateral position on a specially designed table-mounted bicycle ergometer. The initial workload was 30 Watts with increments of 20 Watts every 3 min. At the end of each stage, the heart rate, systolic blood pressure and a 12-lead ECG were recorded. Also, at the end of each step, standard parasternal and apical echocardiographic images containing TDE information were obtained and digitally stored.

Stress echocardiography
Before exercise was started, a two-dimensional ECG with superimposed TDE images was performed using a 3.5 MHz transducer with commercially available equipment (System FiVe™; GE Vingmed, Horten, Norway). Standard parasternal short- and long-axis views as well as apical two-, three- and four-chamber views were digitized during two consecutive cardiac cycles in cine-loop format for off-line analysis.

Off-line analyses
All echocardiographic images were analysed off-line using specially designed software (Echopac™ 6.3.4; GE Vingmed) for calculation of TDE variables. The LV was divided into 16 segments (six basal segments, six mid-ventricular segments and four apical segments). The six basal segments were designated as follows: septal, lateral, inferior, posterior, anterior and antero-septal. The LV short-axis systolic and diastolic functions were assessed from the parasternal long- and short-axis images, from which only the inferior (parasternal short-axis image) and posterior segments (parasternal long-axis image) were able to be analysed. The LV long-axis function was assessed from the apical views from which six LV basal segments were analysed. A sample volume was positioned in the region of interest to obtain a tissue velocity profile during two cardiac cycles. Both systolic and diastolic phases of the velocity profile were considered for analysis. The following parameters were analysed (Figure 1): isovolumic contraction time (IVCT, in ms), measured from the Q-wave of the monitoring ECG lead to the beginning of ejection on the velocity profile; isovolumic relaxation time (IVRT, in ms), measured from the end of ejection time until the start of the E-wave; peak systolic velocity (PSV, in cm/s), measured at the peak velocity during ejection; peak velocity at early diastole (E′-wave, in cm/s), measured at the peak velocity of the early diastolic wave; peak velocity at late diastole (A′-wave, in cm/s), measured at the peak velocity of the late diastolic wave. The myocardial wall excursion (mm) in long- and short-axis was obtained by automated temporal integration of the velocity profile of the basal segments during ejection.

Statistical analyses
Data are presented as means ± S.D. ANOVA with repeated measures was used to test statistical significance.
of the studied variables during different workloads. A $P$ value of $<0.05$ was considered statistically significant. When ANOVA showed statistically significant differences among all workloads, post-hoc analysis with Bonferroni’s test was performed to assess differences between workloads.

**RESULTS**

All standard echocardiographic data were within normal reference range (Table 1). With the increase in workload (from rest until 70 Watts), there was a successive decrease in the RR interval as well as in IVCT and IVRT measured from the short- and long-axis (Tables 2 and 3). PSV gradually increased during successive workload increments in both long- and short-axis directions (Tables 2–4, and Figure 2a). The long-axis myocardial excursion of the base of the heart rapidly increased from rest to 30 Watts and thereafter reached a plateau; on the other hand, the short-axis myocardial excursion increased continuously during successive increments of the workload (Tables 2 and 3, and Figure 2b). Resting $E'/A'$ ratio, measured from the short-axis velocity profile, was $>1$; however, an inverted $E'/A'$ ratio ($<1$) was observed when measured from the long-axis. The velocities of $E'$- and $A'$-waves increased progressively with successive increments in workload, both in the long- and short-axis, resulting in restoration of the long-axis $E'/A'$ ratio

![Image](image-url)
to a ’normal’ level during stress (Tables 2 and 3), without altering the short-axis E’/A’ ratio. Figure 3 shows the results of regression analysis between the PSV and the RR interval performed for each individual on the basis of the results obtained at rest and at each stage of exercise. The Figure shows the possible relationship between the increments in PSV and increments in heart rate (represented by shortening of the RR interval).

**DISCUSSION**

The main findings of the present study are: (i) the increase in the basal myocardial long-axis velocity with successive increments of exercise workload is more dramatic compared with that observed in short-axis; (ii) long-axis myocardial excursion occurs mostly in the initial phase of exercise, whereas the short-axis excursion progresses steadily throughout the exercise duration; (iii) the myocardial velocity and excursion response is, by and large, influenced by the chronotropic behaviour of the heart; and (iv) long- and short-axis diastolic data differ considerably, signifying that diastolic filling of the LV is probably a matter of stretching of the longitudinal fibres. The concept is supported by the fact that long-axis E’/A’ ratio increases gradually with increasing workloads, whereas that in short-axis remains practically unchanged. The diastolic data also show that the change of E’/A’ ratio with aging is a physiological process [10], and that this process can be reverted during exercise in healthy elderly people.

The present findings have not been reported previously and may have some clinical relevance when interpreting stress echocardiography by quantitative means. In a study of young healthy individuals, a continuous increment in PSVs in long-axis has been reported [11]. However, the behaviour of the longitudinal and circumferential excursion was not described. In the light of the results of the present study, it is important to note that the lack of a further increment in the myocardial long-axis

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**Table 2** Echocardiography variables (time intervals, velocities and excursions) reflecting short-axis LV function measured at rest and during exercise
The values are the average of the inferior wall and the posterior walls. Values are means ± S.D. *P < 0.01 compared with value at rest; † P < 0.01 compared with the value at 30 Watts.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Rest</th>
<th>30</th>
<th>50</th>
<th>70</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR interval (ms)</td>
<td>891 ± 154</td>
<td>659 ± 110*</td>
<td>585 ± 82†</td>
<td>541 ± 86†</td>
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<tr>
<td>IVCT (ms)</td>
<td>72 ± 18</td>
<td>64 ± 19</td>
<td>54 ± 15</td>
<td>52 ± 15</td>
</tr>
<tr>
<td>IVRT (ms)</td>
<td>31 ± 10</td>
<td>28 ± 8</td>
<td>26 ± 7</td>
<td>24 ± 5</td>
</tr>
<tr>
<td>PSV (cm/s)</td>
<td>4.13 ± 1.78</td>
<td>4.48 ± 1.11</td>
<td>5.20 ± 1.44</td>
<td>5.95 ± 1.43†</td>
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<tr>
<td>Short-axis excursion (mm)</td>
<td>5.02 ± 1.83</td>
<td>6.03 ± 1.73</td>
<td>6.55 ± 2.06</td>
<td>6.78 ± 1.63†</td>
</tr>
<tr>
<td>E’-wave (cm/s)</td>
<td>4.74 ± 1.88</td>
<td>5.23 ± 1.41</td>
<td>6.40 ± 1.99†</td>
<td>6.87 ± 2.41†</td>
</tr>
<tr>
<td>A’-wave (cm/s)</td>
<td>3.74 ± 1.55</td>
<td>4.33 ± 1.68</td>
<td>4.61 ± 1.60</td>
<td>5.32 ± 1.52*</td>
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<tr>
<td>E’/A’ ratio</td>
<td>1.26 ± 0.12</td>
<td>1.20 ± 0.08</td>
<td>1.38 ± 0.12</td>
<td>1.29 ± 0.15</td>
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</tbody>
</table>

**Table 3** Echocardiographic variables (time intervals, velocities and excursions) reflecting long-axis LV function measured at rest and during exercise
The values are the average of the six LV walls registered from the apical 4- and 2-chamber views as well as the apical long-axis view (postero-septal, lateral, inferior, anterior, posterior and antero-septal). Values are means ± S.D. *P < 0.01 compared with value at rest; † P < 0.01 compared with the value at 30 Watts; †† P < 0.01 compared with the value at 50 Watts.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Rest</th>
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<th>50</th>
<th>70</th>
</tr>
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<tr>
<td>RR interval (ms)</td>
<td>900 ± 155</td>
<td>618 ± 106*</td>
<td>539 ± 95†</td>
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<td>IVCT (ms)</td>
<td>85 ± 9</td>
<td>54 ± 8</td>
<td>48 ± 7†</td>
<td>44 ± 6†</td>
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<tr>
<td>IVRT (ms)</td>
<td>77 ± 10</td>
<td>43 ± 9</td>
<td>38 ± 7</td>
<td>35 ± 6†</td>
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<td>PSV (cm/s)</td>
<td>6.41 ± 1.21</td>
<td>8.41 ± 1.26*</td>
<td>9.63 ± 0.93†</td>
<td>10.72 ± 1.08††</td>
</tr>
<tr>
<td>Long-axis excursion (mm)</td>
<td>10.16 ± 1.85</td>
<td>13.16 ± 1.39*</td>
<td>13.29 ± 1.90*</td>
<td>13.37 ± 1.56*</td>
</tr>
<tr>
<td>E’-wave (cm/s)</td>
<td>6.46 ± 1.46</td>
<td>9.90 ± 1.79*</td>
<td>11.77 ± 2.54†</td>
<td>12.73 ± 2.80†</td>
</tr>
<tr>
<td>A’-wave (cm/s)</td>
<td>7.93 ± 1.30</td>
<td>10.77 ± 1.89*</td>
<td>11.95 ± 2.41*</td>
<td>12.55 ± 2.38†</td>
</tr>
<tr>
<td>E’/A’ ratio</td>
<td>0.81 ± 0.11</td>
<td>0.91 ± 0.09</td>
<td>0.98 ± 0.1</td>
<td>1.01 ± 0.09*</td>
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</table>
Excursion during later phases of exercise is not a pathological phenomenon. On the contrary, increments of myocardial excursion in the short-axis support the clinical observations of radial thickening (endocardial excursions) and a continuous decrease in LV cavity size noted during peak stages of stress echocardiography in the absence of wall motion abnormality.

The small and non-statistically significant increase in PSV and excursion in the short-axis may be interpreted as a result of an underpowered sample size. As the present study had an explorative character, no sample size was calculated, but a post-hoc analysis (type I error, 0.05; power, 0.8) showed that > 270 individuals were necessary to show statistically significant differences in PSV between rest and 30 Watts, > 50 between 30 and 50 Watts, and > 57 between 50- and 70 Watts. However, with the actual sample size, statistically significant differences were found between rest and 70 Watts. Even larger numbers were necessary to detect statistically significant differences in short-axis excursion at low workloads. The large sample size required to detect statistically significant changes at low workloads implies that those changes are clinically irrelevant.

Longitudinal and radial functions of the heart

In the LV, the myocardial circumferential fibres occupy the basal and middle segments, whereas the longitudinal fibres are found in the subendocardium, subepicardial free wall as well as the papillary muscles [12]. The larger part of the myocardial mass is composed of the circumferential fibres, whereas the longitudinal fibres constitute only a small part of the LV muscle mass [12]. It is therefore logical to derive information on the underlying cardiac function by functional quantification of the circumferential fibres. However, the function of the heart is complex and only 25–40% of the decrease in the LV short-axis dimensions during systole can be explained on the basis of the combined action of the longitudinal and circumferential fibres [13]. Without the longitudinal component, normal sarcomere shortening would contribute to a fractional shortening of 12% and an ejection fraction of 30% [13]. What we have found in the present study is that during exercise the initial contribution of the left ventricle to meet the physiological demands of the heart comes from the subendocardial longitudinal fibres of the heart, whereas, once the initial take-off has taken place, the left ventricle brings the circumferential fibres into the contractile process to continue to increase the stroke output in the face
of increasing demand. Although we have no data to corroborate this type of functional switch-over, it is in close agreement with the observation made by grey-scale imaging during routine stress echocardiography. This switch-over may be protective for the heart, because subendocardial fibres are more sensitive to myocardial ischaemia and probably are the first fibres that become ischaemic when an imbalance in coronary blood supply/demand occurs [14].

As shown in Tables 2 and 3, most of the changes in heart rate and in IVCT and IVRT occurred during the initial phase of exercise. Those changes mirrored the changes in myocardial excursion in both directions and the changes in velocities in the long-axis (Figure 2). Our explanation for this finding is that heart rate is closely correlated with myocardial PSV and excursion both intrinsically and through its positive inotropic effect (treppe effect; [15,16]). Recently, Cain et al. [17] in a group of 179 patients without regional abnormal wall motion did not find any correlation between heart rate and LV long-axis myocardial velocities; however, the statistical analysis in that study was done on the whole population at different stages of dobutamine infusion and did not take into account the changes in systolic velocity induced by changes in heart rate for every patient, as in fact was performed in the present study. In the MYDISE (Myocardial Doppler in Stress Echocardiography) study, a moderate association was found between PSV and heart rate in normal subjects at peak dobutamine stress [2].

In a previous animal study [18], PSV decreased after intravenous $\beta$-blockade, and no additional decrement was observed when the animals were paced at heart rates slightly higher than the baseline. On the basis of these findings, the authors [18] concluded that the decrease in PSV was independent of the fall in heart rate induced by $\beta$-blockade. This study [18] indicates that the treppe effect on myocardial PSV is small compared with the influence of the sympathetic nervous system on contractility.

The strong correlation between the increments in heart rate and the increments in PSV and excursion during exercise stress echocardiography emphasizes the fact that, when interpreting the myocardial PSV and excursion data, the achieved peak heart rate has to be taken into account.

Patients with suspected and known coronary artery disease are usually treated with $\beta$-adrenergic blocking agents or calcium antagonists, both of which affect the peak heart rate during exercise. We therefore propose that nullification of myocardial PSV and excursion by heart rate could be a classic finding of normally functioning left ventricle.

### Study limitations

LV short-axis function was assessed by measuring PSVs and excursion from two basal segments, whereas long-axis function was assessed by averaging the values of six basal segments. In other words, we assume that the behaviour of those segments represent the working form of the whole left ventricle. This limitation is part of the
method because, from the parasternal short- and long-axis projections, only those segments are obtainable and analysable. From these projections it is also possible to assess the basal anterior septum and the basal anterior segment; however, the movement of the anterior septum is rather complicated, is affected by the haemodynamics of the right ventricle and TDE-derived measurements of that segment are inaccurate [19]. This fact was confirmed by the finding of a weaker relationship between PSV and heart rate assessed in the short-axis, indicating that measuring PSV and displacement in the short-axis during exercise is technically demanding. It has to be acknowledged that assessing the LV short-axis function from the basal inferior and posterior segments (registered from the parasternal short- and long-axis) may also imply the possibility of measuring a combination of longitudinal, radial and circumferential, rather than the pure circumferential, LV function. We have therefore utilized the more descriptive terms of long- and short-axis myocardial velocities and displacement that refer to an echocardiographic technique, rather than radial, circumferential and longitudinal myocardial velocities and excursion that refer to physiological phenomena.

Due to the lack of standardization, IVCT was measured from the beginning of QRS complex, including therefore the electromechanical delay interval. This period should more properly be named the ‘pre-ejection period’. Assigning the beginning of the QRS complex as the start of the IVCT, however, facilitated its measurement during exercise and gave reproducible results.

Conclusions
During supine exercise, LV long- and short-axis function seems to behave in different ways. Changes during early exercise in the long-axis appear to be more remarkable, whereas, during the last stage of exercise, changes in the short-axis seem to be more physiologically relevant. LV long- and short-axis function is paralleled by the changes in the heart rate occurring during the early phase of exercise. These facts have to be taken into account to interpret the quantitative echocardiographic findings during exercise stress echocardiography.

References