

Applied Cardiopulmonary Pathophysiology 16: 37-54, 2012

## Physiological systolic and diastolic changes of the left and right heart during exercise stress echocardiography

Stefan A. Lange<sup>1</sup>, Martin U. Braun<sup>2</sup>, Jens Jung<sup>3</sup>

<sup>1</sup>Medizinische Klinik I, Kardiologie und Angiologie, Asklepios Harzklinik Goslar, Akademisches Lehrkrankenhaus der Johannes-Gutenberg-Universität, Göttingen, Germany; <sup>2</sup>Medizinische Klinik I, Kardiologie, Elektrophysiologie und Intensivmedizin, Klinikum Bamberg, Akademisches Lehrkrankenhaus der Friedrich-Alexander-Universität, Erlangen-Nürnberg, Germany; <sup>3</sup>Medizinische Klinik I, Kardiologie und Angiologie, Klinikum Worms, Akademisches Lehrkrankenhaus der Johannes-Gutenberg-Universität, Mainz, Germany

### Abstract

**Objective:** The aim of this study was to evaluate echocardiography parameters of the left and right heart function during exercise.

**Methods:** We studied 20 healthy, normal trained volunteers (10 male). All participants underwent an echocardiography at rest and during exercise.

**Results:** At peak exercise, higher echocardiography values were achieved in men for the tissue Doppler imaging (TDI)  $s'$  at the mitral valve annulus (MVA). During exercise, peak early diastolic filling velocity (E Vmax), peak late diastolic filling velocity (A Vmax), and pulmonary vein flow increased significantly. E/A ratio, deceleration time (DT) and isovolumic relaxation time (IVRT) decreased significantly. The TDI velocities  $e'$  and  $s'$  (MVA) increased significantly.

There were linear correlations between workload (METS) and the mitral and pulmonary vein flow, the ratios of diastolic filling (E/ $e'$ ) and the TDI velocities (MVA). The best correlation was obtained for METS and  $s'$  ( $r^2=0.5$ ).

During exercise, parameters of the right heart e.g. the tricuspid annulus plane systolic excursion and the TDI parameters at the lateral tricuspid valve annulus (TVA)  $e^a$  and  $s^a$  increased significantly. The right ventricular systolic pressure (RVSP) increased during exercise but stayed in a normal range.

There were linear correlations between workload and  $e^a$ ,  $s^a$ , TAPSE and RVSP. The best correlation was achieved for METS and  $s^a$  ( $r^2 = 0.49$ ).

**Conclusion:** Systolic and diastolic parameters of the left and right heart changed during exercise in relation to workload, but E/ $e'$  ratio and RVSP stayed in a normal range.

**Key words:** exercise stress echocardiography, tissue doppler imaging, right heart function, left heart function, workload

### Introduction

During the last two decades the prevalence of diastolic heart failure has increased from 38% to 54% of all heart failure cases (1, 2).

The diagnosis of heart failure with normal ejection fraction is based on physical examination with signs of heart failure, normal or mildly reduced left ventricular systolic function and the evidence of abnormal LV relax-

ation, filling, diastolic distensibility, and diastolic stiffness. Determinants for detailed diagnostic of diastolic heart failure are invasive hemodynamic measurements, biomarkers (e.g. NT-proBNP), and special echocardiography parameters (e.g. TDI of annular and myocardial motion and pulse wave Doppler of the mitral and pulmonary vein flow) (3-5). Patients with the complete picture of diastolic heart failure were characterized simply by these tools (6, 7). To detect patients with onset of diastolic dysfunction is often more difficult but still relevant.

Techniques disclosing subclinical diastolic impairment could be measurements of flow velocity of mitral inflow and pulmonary vein flow as well as TDI of the mitral annulus during ergometric exercise. Stress echocardiography is a commonly accepted method to reveal relevant ischemic coronary heart disease and to describe also systolic and diastolic myocardial function (8, 9). Off-line Tissue Doppler measurements of the left ventricle are also practicable to describe regional left ventricular function during exercise and dobutamine stress echocardiography (10-12).

In the last decade the function of the right heart has come into the focus of interest e.g. in case of secondary pulmonary hypertension. The process of contraction of the right ventricle differs importantly to the left ventricle and the evaluation of right ventricular volume and ejection fraction by standard two-dimensional echocardiography is complicated because of the endocardial surfaces and the half-moon shape of the right ventricle (13, 14). A not unchallenged attempt to evaluate contraction quality of the right heart was the M-mode measurement of the tricuspid annular plane systolic excursion (TAPSE) (15-18).

Doppler Tissue imaging of the tricuspid annular motion is a way of classifying right ventricular function. There is a good correlation between systolic annular velocity and right ventricular function in different right heart diseases (19-23). In patients with symptomatic heart failure systolic and diastolic TDI

tricuspid annular motions are independent predictors of event-free survival (24).

The following study focused on the physiological alterations in systolic and diastolic flow and tissue velocities of the left and especially of the right ventricle during stress exercise testing in dependence of workload.

In the future these values should provide a basis for comparison to stress echo values in patients with pulmonary hypertension to characterize their right heart limitations or their right heart reserve under exercise conditions, and in patients of an incipient diastolic heart failure to help physicians for their therapeutic decisions.

## Material and methods

All echocardiography explorations were performed with conventional echocardiography system (General electric GE Vivid 7 Dimension and a cardiac transducer 1.5 – 4.0 MHz, Medical Systems, Norway). All the measurements were taken by a single investigator.

Before study inclusion, each volunteer obtained a complete medical assessment and received a trans-thoracic two dimensional echocardiography. We included in this study ten male and ten female volunteers (Caucasian race) without chronic or acute illness and in normal or good physical condition with normal echocardiography parameters at rest. Informed consent was obtained of each volunteer.

The volunteers underwent bicycle stress testing in half sitting position (30-45°) with left incline of 45 degree (Ergometrics 900, Ergoline, D-72475 Bitz, Germany). The stress testing was based on a modified Bruce protocol: The ergometric load started with 25 watts and increased every 3 min by 25 watts. Before and during exercise (in the third minute), we measured blood pressure, heart rate and the following echocardiography parameters of the LV inflow (pulse wave Doppler: peak early diastolic filling velocity (E Vmax), peak late diastolic filling velocity (A

Vmax), transmitral velocities, Isovolumic Relaxation Time (IVRT), the inflow of the right upper pulmonary vein (pw Doppler: the pulmonary systolic flow velocity (sPV), the pulmonary diastolic flow velocity (dPV), and the atrial reversal (AR), and parameters of the right ventricle (M-mode: the tricuspid annulus plane systolic excursion (TAPSE) and the right ventricle systolic pressure (RVSP) with continuous wave (cw) Doppler. We assessed the valve insufficiency of the mitral and tricuspid valve during exercise (color Doppler). Echocardiography parameters were chosen for semi quantification of valve regurgitation or stenosis according to AHA guidelines. We also allowed intermediate degrees (e.g. 0-1°, 1-2°). The chamber quantifications at rest were in accordance to the American Society of Echocardiography and the European Association of Echocardiography (14). Finally, the tissue Doppler imaging (TDI) records of the lateral and septal mitral valve annulus (early annular velocity,  $e'$  and systolic motion,  $s'$ ), and for the lateral tricuspid valve annulus (tricuspid early annular velocity,  $e^a$ , and tricuspid annular systolic motion,  $s^a$ ) were determined. The inter-observer variability for peak systolic velocities at peak dose of dobutamine were lowest at the basal septal and basal lateral segments, so we decided to take only values from these basal segments in the apical four chamber view (10). When  $e$  and  $a$  waves were fused at rapid heart rates, then a single diastolic velocity ( $e'$ ,  $e^a$ ) was measured (10).

To reduce intra observer variability during exercise we calculated online seven consecu-

tive hearts cycles (if available) and calculated the mean values afterwards.

## Statistics

Values are means  $\pm$  standard error of means (SEM). Two-way ANOVA with repeated measurements were used to test for differences between gender and watts and physical parameters at rest and during exercise, echocardiography values of the left and right heart at rest and at exercise peak levels. In cases with no significant gender specific differences of the echocardiography parameters we compared the combined male and female parameters at rest and during exercise. Bivariate and partial Pearson-correlation test showed the correlations among these values. A probability value of less than 0.05 was considered to be statistically significant. The statistic measurements were performed by SigmaPlot 11.2

## Results

**Comparison of basic parameters between male and female:** The mean age for the male and female group did not differ significantly. The body surface area in male was higher than in the female as expected. Heart rate at rest did not differ significantly between men and women. Blood pressures at rest for systolic and diastolic parameters were not significantly different in both genders (Table 1).

Table 1: Comparison of basic parameters at rest

Parameter	Male mean value $\pm$ SEM	Female mean value $\pm$ SEM	p-value
Mean age	27.6 years	31.3 years	ns.
Body surface area	2.04 $\pm$ 0.05 m <sup>2</sup>	1.80 $\pm$ 0.04 m <sup>2</sup>	<0.0001
Systolic blood pressure	115.6 $\pm$ 3.4 mmHg	119.1 $\pm$ 7.0 mmHg	ns.
Diastolic blood pressure	76.6 $\pm$ 3.4 mmHg	74.1 $\pm$ 3.4 mmHg	ns.
Heart rate	73 $\pm$ 6 min <sup>-1</sup>	83 $\pm$ 4 min <sup>-1</sup>	ns.

Table 2: Comparison of the echocardiography parameters of the left heart at rest

Parameter	Male mean value $\pm$ SEM	Female mean value $\pm$ SEM	p-value
Left atrium Index (LAI)	17.4 $\pm$ 0.6 mm/m <sup>2</sup>	17.8 $\pm$ 0.71.5 mm/m <sup>2</sup>	ns.
Left ventricle end diastolic diameter index (LVEDDI)	25.5 $\pm$ 0.6 mm/m <sup>2</sup>	25.7 $\pm$ 0.6 mm/m <sup>2</sup>	ns.
Left ventricle end systolic diameter index (LVESDI)	15.4 $\pm$ 0.4 mm/m <sup>2</sup>	15.6 $\pm$ 0.7 mm/m <sup>2</sup>	ns.
Intraventricle septum (end systolic, IVS)	9.5 $\pm$ 0.3 mm	8.8 $\pm$ 0.4 mm	ns.
Posterior wall (end systolic, LVPW)	9.6 $\pm$ 0.3 mm	8.8 $\pm$ 0.3 mm	ns.
Aortic root index (Aoi)	16.0 $\pm$ 0.5 mm/m <sup>2</sup>	15.4 $\pm$ 0.5 mm/m <sup>2</sup>	ns.
LA volume index (LAVI)	21.5 $\pm$ 2.3 ml/m <sup>2</sup>	18.2 $\pm$ 1.8 ml/m <sup>2</sup>	ns.
LV diastolic volume index (LVDVI)	45.4 $\pm$ 2.3 ml/m <sup>2</sup>	40.4 $\pm$ 2.9 ml/m <sup>2</sup>	ns.
LV systolic volume index (LVSVI)	16.6 $\pm$ 0.9 ml/m <sup>2</sup>	12.2 $\pm$ 1.1 ml/m <sup>2</sup>	<0.05
Cardiac output (Simpson biplane)	4.39 $\pm$ 0.58 l/min	4.22 $\pm$ 0.39 l/min	ns.
peak early diastolic filling velocity (E Vmax)	86.0 $\pm$ 7.7 cm/s	101.0 $\pm$ 5.5 cm/s	ns.
peak late diastolic filling velocity (A Vmax)	45.7 $\pm$ 3.8 cm/s	67.6 $\pm$ 7.6 cm/s	<0.05
E/A ratio	2.0 $\pm$ 0.3	1.64 $\pm$ 0.17	ns.
Deceleration time (DT)	199.0 $\pm$ 18.1 cm/s	174.0 $\pm$ 8.0 cm/s	ns.
Isovolumic relaxation time (IVRT)	94.0 $\pm$ 4.7 ms	77.0 $\pm$ 5.2 ms	<0.05
systolic Pulmonary vein flow (sPV)	53.0 $\pm$ 3.5 cm/s	59.0 $\pm$ 3.7cm/s	ns.
diastolic Pulmonary vein flow (dPV)	68.2 $\pm$ 5.6 cm/s	66.0 $\pm$ 3.3 cm/s	ns.
Atrial reversal (AR)	27.0 $\pm$ 1.5 cm/s	32.0 $\pm$ 1.6 cm/s	ns.
e' (early annular velocity) lateral MVA	20.1 $\pm$ 1.2 cm/s	18.3 $\pm$ 2.7 cm/s	ns.
e' (early annular velocity) septal MVA	13.9 $\pm$ 1.0 cm/s	17.4 $\pm$ 1.0 cm/s	ns.
e' (early annular velocity) average	17.0 $\pm$ 1.0 cm/s	17.8 $\pm$ 0.6 cm/s	ns.
s' (systolic motion) lateral MVA	13.0 $\pm$ 1.0 cm/s	13.2 $\pm$ 1.1 cm/s	ns.
s' (systolic motion) septal MVA	9.8 $\pm$ 0.6 cm/s	9.4 $\pm$ 0.7 cm/s	ns.
s' (systolic motion) average	11.4 $\pm$ 0.7 cm/s	11,3 $\pm$ 0.8 cm/s	ns.
E/e' (average) ratio	5.1 $\pm$ 0.3	5.7 $\pm$ 0.3	ns.
Mitral valve insufficiency degree (MI)	0.0	0.3 $\pm$ 0.2	ns.
Tricuspid valve insufficiency degree (TI)	0.45 $\pm$ 0.16	0.45 $\pm$ 0.14	ns.

Table 3: Comparison of the echocardiography parameters of the right heart at rest

Parameter	Male mean value $\pm$ SEM	Female mean value $\pm$ SEM	p-value
Right atrium (RA)	40.2 $\pm$ 1.6 mm	34.3 $\pm$ 1.3 mm	<0.01
Right ventricle (end diastolic, RV)	22.8 $\pm$ 1.2 mm	23.4 $\pm$ 1.4 mm	ns.
RV Tei Index	0.27 $\pm$ 0.04	0.32 $\pm$ 0.03	ns.
Tricuspid annulus plane systolic excursion (TAPSE)	27.3 $\pm$ 0.7 mm	28.3 $\pm$ 1.2 mm	ns.
e <sup>a</sup> annular velocity TAM	15.4 $\pm$ 0.7 cm/s	16.8 $\pm$ 0.8 cm/s	ns.
s <sup>a</sup> motion TAM	14.8 $\pm$ 0.6 cm/s	15.5 $\pm$ 0.2 cm/s	ns.
Right Ventricular Systolic Pressure (RVSP)	14.7 $\pm$ 1.5 mmHg	17.8 $\pm$ 2.5 mmHg	ns.
Vena cava inferior (VCI)	10.9 $\pm$ 1.0 mm	7.5 $\pm$ 0.8 mm	p < 0.01

**Comparison of echocardiography parameters at rest between genders:** No gender differences were detected for LA and LV diastolic volumes corrected by body surface area (BSA), neither for cardiac output (CO) assessed by Simpson's biplane rule.

The diastolic parameters of the left ventricle at rest were subsumed in Table 2.

In the right heart, the right atrium diameter was significantly smaller in females, whereas the parameters of right ventricle size and RV function, for example the RV Tei Index, the TAPSE, the tissue Doppler imaging of the tricuspid annulus motion (TAM) (e<sup>a</sup> and s<sup>a</sup>) did not differ significantly between males and females. The Vena cava inferior (VCI) was larger in male volunteers, but the right ventricular systolic pressure (RVSP) at rest was similar in both genders and in a normal range (Table 3).

**Comparison of exercise stress testing between genders:** Women reached a mean performance of 137.5  $\pm$  6.7 watts with a minimum of 100 watts and maximum of 175 watts. Men reached a higher mean performance of 197.5  $\pm$  5.8 watts with a minimum of 175 watts and a maximum of 225 watts (p < 0.0001).

Heart rate was continuously controlled by ECG. The target frequency was 80% of the maximal heart rate calculated by the formula 220 minus age. In the female group 7 of 10 reached the individual sub maximal heart rate whereas in the male volunteer group only 6 of 10 reached the sub maximal heart rate. The mean heart frequency ratio in the male vs. female group was 87.2% vs. 84.7% of the calculated maximal heart rate. Nobody reached the individual maximum heart rate. The main reason for stopping the test was exhaustion except in one subject that experienced joint knee pain.

The systolic and diastolic blood pressure and the maximum heart rate are shown in Table 4. Significant differences between genders were obtained for diastolic blood pressure.

During exercise testing subsequent echocardiography parameters were different between both genders at peak levels: A Vmax, AR, TDI systolic motion of the septal and lateral MVA (s'), and TDI systolic motion of the lateral tricuspid annulus (s<sup>a</sup>).

**Comparison of parameters during exercise:** Mean blood pressure increased slightly but significantly. As expected, heart rate (HR) increased with increasing exercise.

Table 4: Comparison of the physical exercise parameters

Parameters at peak exercise level	Male mean value $\pm$ SEM	Female mean value $\pm$ SEM	p-value
Systolic blood pressure (SBP)	183 $\pm$ 8 mmHg	170 $\pm$ 12 mmHg	ns.
Diastolic blood pressure (DBP)	63 $\pm$ 6 mmHg	80 $\pm$ 4 mmHg	< 0.05
Heart rate (HR)	161 $\pm$ 7 min <sup>-1</sup>	156 $\pm$ 6 min <sup>-1</sup>	ns.

*Systolic and diastolic parameters of the left ventricle:* During exercise, Doppler velocities of the left heart in both gender changed significantly: E-Vmax and AVmax as well as sPV and dPV increased, while E/A ratio, DT, and IVRT decreased significantly.

The TDI records of the lateral and septal MVA increased also significantly. The E/e' ratio increased slightly but significantly (Table 5).

The increase of E Vmax during exercise correlated significantly positively to the increase of heart rate, A Vmax, sPV, dPV, AR, e', s' as well as negatively to shortening of DT and IVRT (Table 7). Significant linear regressions could be also shown between workload (METS) and the diastolic filling parameters (E Vmax,  $r^2 = 0.42$ , Figure 1a, A Vmax,  $r^2 = 0.31$ , Figure 1b), DT,  $r^2 = 0.28$ , Figure 1c), IVRT,  $r^2 = 0.37$ , Figure 1d), the diastolic and systolic motion of the mitral annulus (Figure

1e and 1f). The best correlation was obtained between workload and s' (Corr.-Coefficient 0.71;  $r^2 = 0.50$ ).

*Systolic and diastolic parameters of the right ventricle during exercise:* The echocardiography parameters for the right heart during exercise also changed significantly. The right ventricular systolic pressure increased by about 54% but stayed in a normal range. TDI e<sup>a</sup>, s<sup>a</sup> and TAPSE increased significantly (Table 6 and Figure 2-4).

There were correlations between RVSP and e<sup>a</sup> during exercise but no correlations were found for RVSP and TAPSE respectively RVSP and sa (Table 6)

There were significant linear regressions for workload (METS) and parameters of the TDI records of the right ventricle function (e<sup>a</sup>,  $r^2 = 0.45$ , and s<sup>a</sup>,  $r^2 = 0.49$ , Figure 5a and b).

Table 5: Comparison of parameters rest, 25 Watts and during peak exercise of the left heart

Parameters during exercise level	Rest	25 Watts value $\pm$ SEM	Peak		p-value (Holm-Sidak-Method)		
					Rest vs. 25W	Rest vs. max	25W vs. max
E Vmax	94 $\pm$ 5	114 $\pm$ 5	166 $\pm$ 7	cm/s	<0.001	<0.001	<0.001
A Vmax							
male	46.7 $\pm$ 3,8	72.0 $\pm$ 8,6	122.1 $\pm$ 10.3	cm/s	<0.001	<0.001	<0.001
female	67.6 $\pm$ 7,6	96.2 $\pm$ 11,9	151.5 $\pm$ 14.1	cm/s	<0.001	<0.001	<0.001
E/A	1.83 $\pm$ 0.15	1.47 $\pm$ 0.09	1.34 $\pm$ 0.10		=0.066	=0.013	=0.403
DT	187.1 $\pm$ 10.1	191.4 $\pm$ 8.7	116.8 $\pm$ 6.3	ms	=0.69	<0.001	<0.001
IVRT	85.1 $\pm$ 3.8	72.9 $\pm$ 3.7	48.5 $\pm$ 3.2	ms	<0.01	<0.001	<0.001
sPV	56.3 $\pm$ 2.6	72.1 $\pm$ 3.9	76.3 $\pm$ 5.0	cm/s	=0.001	<0.001	=0.317
dPV	66.9 $\pm$ 3.2	74.50 $\pm$ 3.7	81.8 $\pm$ 4.1	cm/s	=0.146	=0.003	=0.084
AR							
male	27.3 $\pm$ 1.5	37.3 $\pm$ 3.6	43.4 $\pm$ 2.6	cm/s	=0.008	<0.001	=0.069
female	32.3 $\pm$ 1.6	38.8 $\pm$ 2.3	57.1 $\pm$ 2.8	cm/s	=0.053	<0.001	<0.001
e' lateral (MVA)	19.2 $\pm$ 0.8	21.7 $\pm$ 0.9	28.3 $\pm$ 1.0	cm/s	=0.013	<0.001	<0.001
e' septal (MVA)	15.7 $\pm$ 0.8	19.1 $\pm$ 1,1	26.2 $\pm$ 1.0	cm/s	=0.004	<0.001	<0.001
e' average (MVA)	17.4 $\pm$ 0.5	20.4 $\pm$ 0.8	27.3 $\pm$ 0.9	cm/s	<0.001	<0.001	<0.001
s' lateral (MVA)							
male	13.0 $\pm$ 1.0	14.9 $\pm$ 0.7	24.6 $\pm$ 1.5	cm/s	0.102	<0.001	<0.001
female	13.2 $\pm$ 1.1	14.4 $\pm$ 0.8	18.0 $\pm$ 1.0	cm/s	=0.325	<0.001	=0.007
s' lateral (MVA) (both genders)	13.1 $\pm$ 0.8	14.6 $\pm$ 0.5	21.3 $\pm$ 1.2	cm/s	=0.073	<0.001	<0.001
s' septal (MVA)							
male	9.8 $\pm$ 0.6	12.1 $\pm$ 0.8	23.1 $\pm$ 1.5	cm/s	=0.102	<0.001	<0.001
female	9.4 $\pm$ 0.7	12.7 $\pm$ 0.9	17.3 $\pm$ 0.9	cm/s	=0.020	<0.001	=0.004
s' septal (MVA) (both genders)	9.6 $\pm$ 0.5	12.4 $\pm$ 0.6	20.2 $\pm$ 1.1	cm/s	=0,006	<0.001	<0.001
s' average (MVA)							
male	11.4 $\pm$ 0.7	13.5 $\pm$ 0.5	23.9 $\pm$ 1.4	cm/s	=0.069	<0.001	<0.001
female	11.3 $\pm$ 0.8	13.5 $\pm$ 0.7	17.7 $\pm$ 0.8	cm/s	=0.051	<0.001	=0.001
s' average (MVA) both genders	11.3 $\pm$ 0.5	13.5 $\pm$ 0.4	20.8 $\pm$ 1.1	cm/s	=0.009	<0.001	<0.001
E/e' average	5.4 $\pm$ 0.2	5.7 $\pm$ 0.3	6.2 $\pm$ 0.3		=0.263	=0,004	=0,051

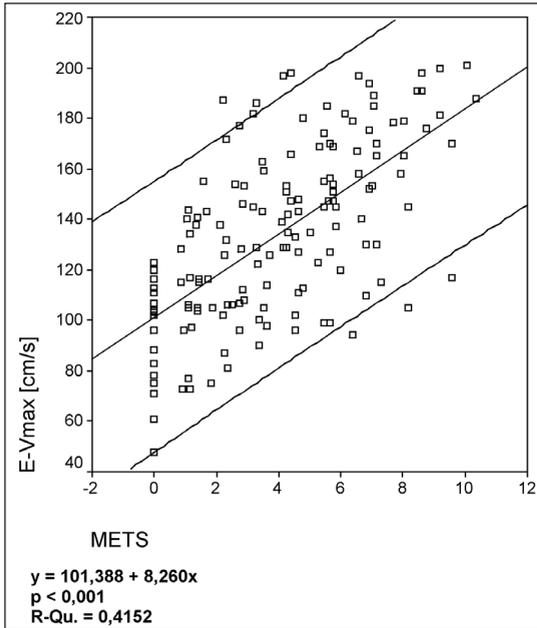


Figure 1a: Linear regression scatter plots for left ventricle E Vmax in dependence of workload (METS)

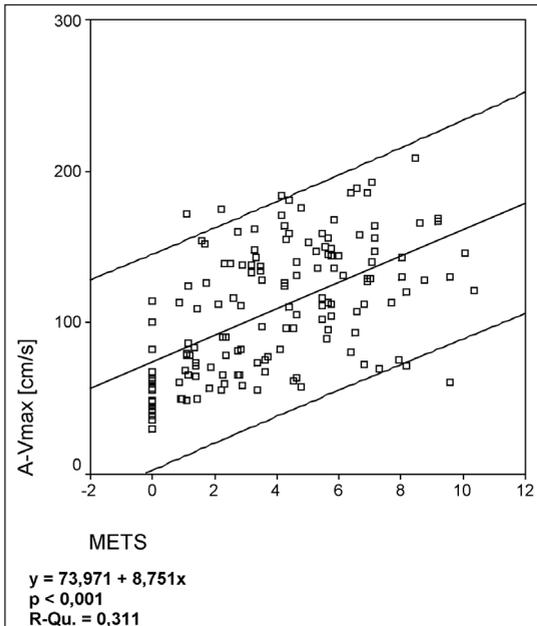


Figure 1b: Linear regression scatter plots for left ventricle A Vmax in dependence of workload (METS)

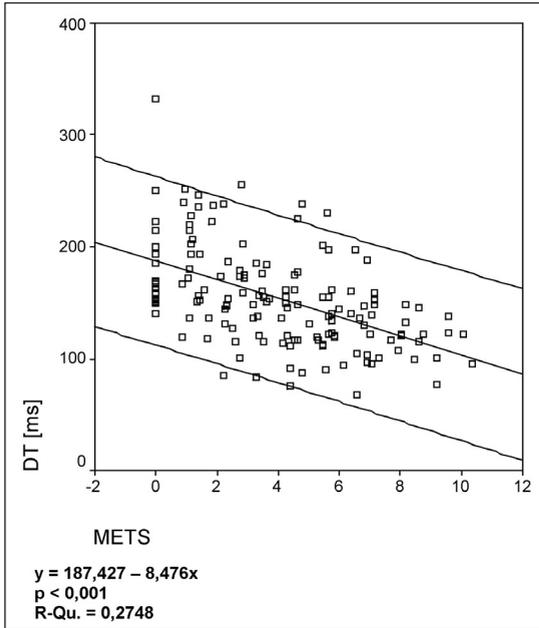


Figure 1c: Linear regression scatter plots for left ventricle DT in dependence of workload (METS)

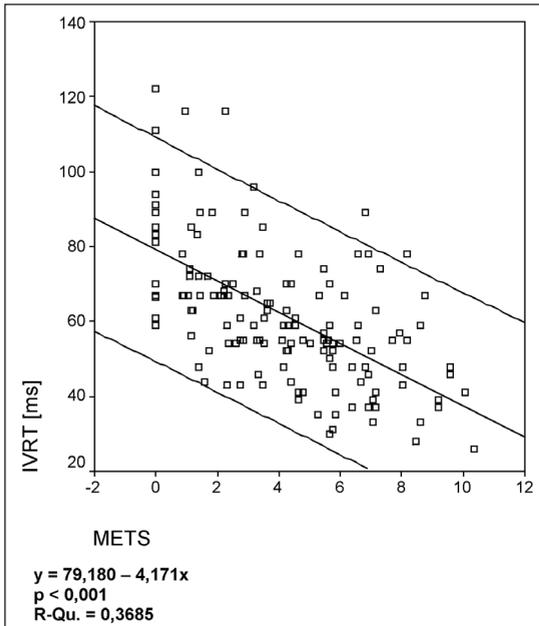


Figure 1d: Linear regression scatter plots for left ventricle IVRT in dependence of workload (METS)

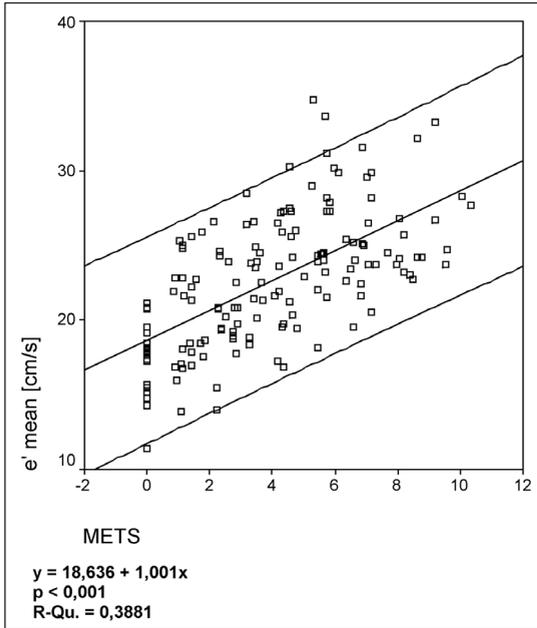


Figure 1e: Linear regression scatter plots for left ventricle diastolic TDI value  $e'$  in dependence of workload (METS)

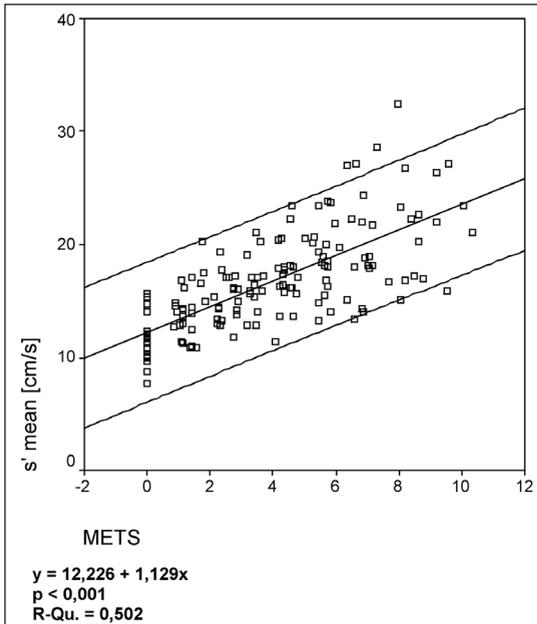


Figure 1f: Linear regression scatter plots for left ventricle systolic TDI values in dependence of workload (METS)

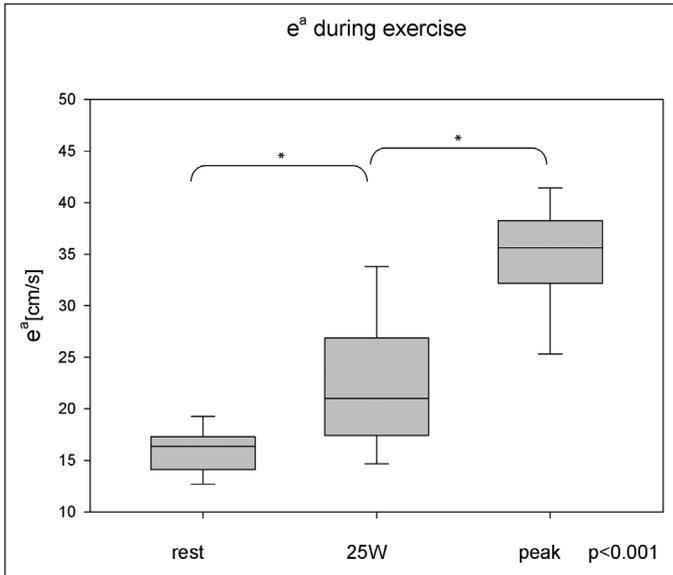


Figure 2: e<sup>a</sup> lateral (TVA) increased during exercise significantly (Two-way RM ANOVA)

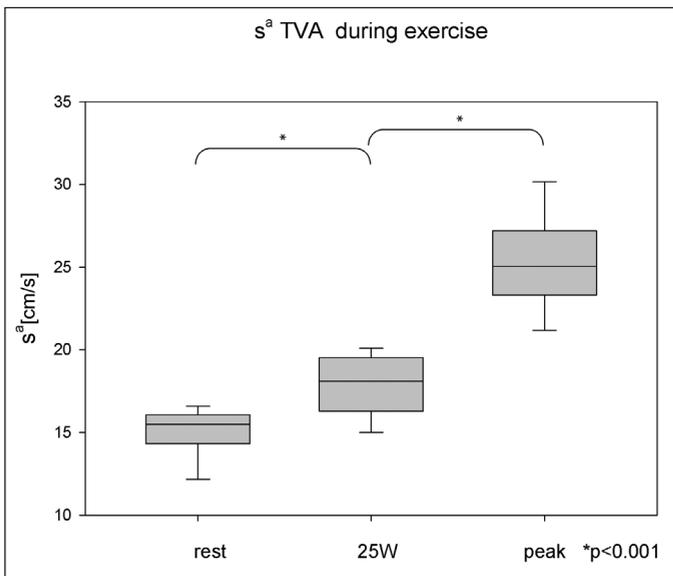


Figure 3: s<sup>a</sup> lateral (TVA) increased during exercise significantly (Two-way RM ANOVA)

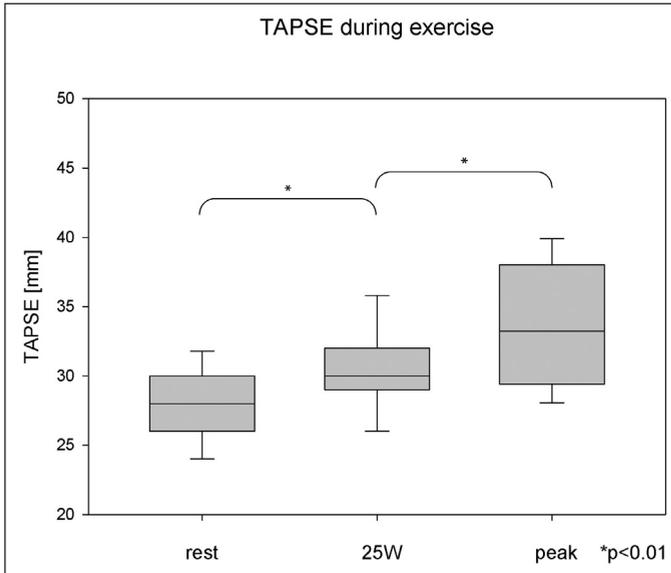


Figure 4: TAPSE increased during exercise significantly (Two-way RM ANOVA)

Table 6a: Comparison of right heart parameters at rest, 25 Watts and during peak exercise

Parameters during exercise level	Rest	25 Watts value $\pm$ SEM	Peak		p-value (Holm-Sidak-Method)		
					Rest vs. 25W	Rest vs. max	25W vs. max
TAPSE	27.8 $\pm$ 0.7	30.6 $\pm$ 0.7	33.7 $\pm$ 1.1	mm	=0.005	<0.001	=0.004
e <sup>a</sup> TAM	16.1 $\pm$ 0.5	22.2 $\pm$ 1.4	35.2 $\pm$ 1.4	cm/s	<0.001	<0.001	<0.001
s <sup>a</sup> TAM							
male	14.8 $\pm$ 0.6	17.5 $\pm$ 0.5	26.7 $\pm$ 1.0	cm/s	=0.007	<0.001	<0.001
female	15.5 $\pm$ 0.2	18.4 $\pm$ 0.6	23.9 $\pm$ 0.8	cm/s	=0,008	<0.001	<0.001
s <sup>a</sup> TAM both genders	15.2 $\pm$ 0.3	18.0 $\pm$ 0.4	25.3 $\pm$ 0.7	cm/s	<0.001	<0.001	<0.001
RVSP	15.7 $\pm$ 1.3	17.5 $\pm$ 1.8	24.2 $\pm$ 1.7	mmHg	=0,130	<0.001	<0.001

Table 6b: Bivariate Pearson correlations of parameters during exercise

	Correlation	p-value (1-side)
E Vmax and HR	0.68	<0.001
E Vmax and A Vmax	0.76	<0.001
E Vmax and IVRT	0.59	<0.001
E Vmax and DT	0.59	<0.001
E Vmax and sPV	0.46	<0.001
E Vmax and dPV	0.45	<0.001
E Vmax and AR	0.45	<0.001
E Vmax and e'	0.51	<0.001
E Vmax and s'	0.33	<0.001
E Vmax and e <sup>a</sup>	0.56	<0.001
E Vmax and s <sup>a</sup>	0.49	<0.001
RVSP and e <sup>a</sup>	0.26	<0.001
RVSP and TI at rest	0.48	<0.05
RVSP and TI peak exercise	0.52	<0.05
TAPSE and s <sup>a</sup>	0.42	<0.001

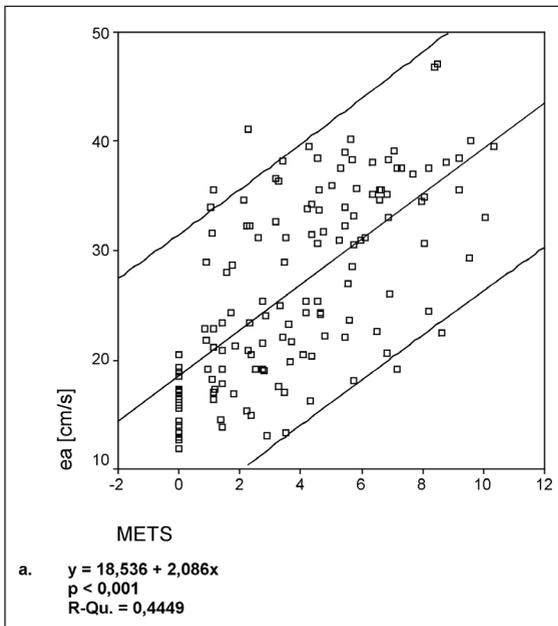


Figure 5a: Linear regression scatter plots for right ventricle diastolic TDI value e<sup>a</sup> in dependence of workload (METS)

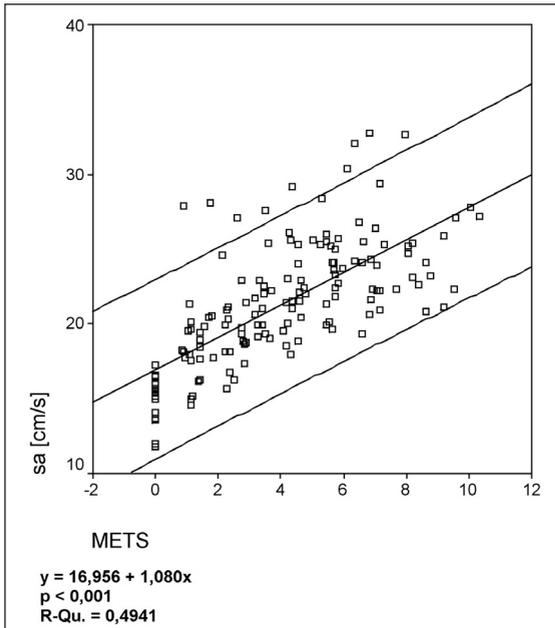


Figure 5b: Linear regression scatter plots for right ventricle systolic TDI value  $s^a$  in dependence of workload (METS)

## Discussion

This study represents an attempt to describe the physiological LV and RV changes during dynamic exercise in a healthy normal trained population, and to correlate them with achieved workload.

The measured echocardiography values at rest adjusted to the body surface area differed significantly only for systolic volume index between gender (14). The diastolic parameters for the mitral inflow showed significant differences between genders in peak late diastolic filling velocity and iso-volumetric relaxation time.

A few parameters of the right heart e.g. the size of the right atrium and the filling pattern of the vena cava inferior were also different between genders.

As expected, the male volunteers reached a higher exercise performance than the female volunteers. Systolic blood pressure increased similarly during exercise in both genders; however the diastolic pressure at peak level was significantly lower in the male group.

In both genders we could show significant changes in diastolic data of the mitral inflow, systolic and diastolic pulmonary vein flow, and tissue Doppler imaging records of the lateral and septal mitral valve annulus during exercise. Most of these parameters increased rapidly during exercise.

Differences between male and female volunteers were only found for a few sampled values, e.g. peak atrial flow velocities, atrial reversal, and the TDI systolic motion  $s'$ . Latter value is well-founded in higher values for the left ventricle mass in men (14).

All diastolic parameters of the left heart changed during exercise: The E Vmax and A Vmax increased, while the E/A ratio, the deceleration time and the IVRT decreased significantly. The systolic and the breathing dependent (25) diastolic pulmonary vein flow as well as the atrial reversal rose significantly. An increase of the E and A flow velocities and an decrease of the E/A ratio was observed in young athletes during a steady-state supine cycling with a maximal heart rate of 100 bpm (26). A higher maximal blood flow velocity of early passive left ventricular filling could be proved also in endurance trained

athletes (9). In contrast, our study obtained values during peak exercise in normal healthy subjects. The TDI parameters also increased. The  $E/e'$  ratio increased slightly but significantly although they remained in a normal range (3, 11). There were some close correlations among these classical diastolic values, but  $E/e'$  (average) ratio seemed to be an independent parameter and correlated closely to filling pressure. Most of these values are volume dependent (27) and alterations may be caused by the increase of the heart volume per time. Systolic tissue velocities at the ventricular base represent the integral of myocardial shortening velocity from base to apex and therefore provide information on global ventricular function (28, 29). The increase of TDI velocities could be caused by an increase of myocardial contractility according to the Frank-Starling-Mechanism and might be a criterion for systolic and diastolic function of the left heart. This hypothesis was supported by the observation that an increase of heart rate alone led to a decrease of mitral valve early flow velocities and mitral annulus early TDI velocities (30). An increase of the TDI parameters of the left ventricle has been described before during isometric leg extension, in children during cycling, in young trained subjects, and also in healthy volunteers during supine and upright exercise (11, 26, 31, 32). In contrast, in diseased hearts as in hypertrophic cardiomyopathy or in patients with diabetes, the normal resting TDI values did not experience further increase during exercise. In patients with congestive heart failure peak systolic and diastolic velocities correlated significantly with maximum exercise capacity (33). Here, all measured parameters correlated significantly with increasing exercise as measured by metabolic equivalents. Here a close correlation was obtained for workload and systolic tissue Doppler motion ( $s'$ ).

Analysis of the echocardiography parameters of the right ventricle function during exercise showed a significant increase of the tricuspid valve annulus plane systolic excursion and the TDI parameters of the tricuspid valve

annulus ( $e^a$  and  $s^a$ ) as well as an increase of the right ventricular systolic pressure (RVSP). There was a close correlation between TAPSE and  $s^a$ . But only a close correlation was obtained for workload and  $e^a$  and  $s^a$ . A study in subjects after marathon running did not show an increase of the RV-TDI velocities, however, these measurements were taken in the convalescence period and not during the exercise (34).

Studies of TAPSE at rest showed a decrease in patients with right and left heart failure as well (15, 16) so this parameter could not differentiate selectively between right or left heart failure. The TDI records for the tricuspid valve annulus correlate with pulmonary hemodynamics (35) and could be better values to describe the right heart function, an increase of  $s^a$  could be a secure sign for a good right ventricular function during exercise (19, 36). But recently published data in patients with hemodialysis showed a preload-dependent of systolic and diastolic RV velocities. These observations delimitate the validity of TDI velocity values at rest (37).

In an unpublished study of our working group we obtained a significant reduction of systolic velocities of the RV at rest after ASD closure, maybe as a result of decreasing right ventricle flow volume, but an adequate increase of these systolic velocities during ergometric cycle. Thus, an adequate increase of RV TDI velocities during exercise in this ASD study could be an argument for the expected preservation of the RV function after ASD closure.

Future studies in patients with normal left and right heart function at rest will verify the ability of stress exercise echocardiography to assess a concealed diastolic and/or systolic dysfunction of the heart and will find out if such a diagnostic approach would be feasible for determining the prognosis. Otherwise pathological heart function under working load could be a hint for further therapy e.g. medical treatment of arterial hypertension or the correction of an acquired or a congenital heart defect.

### Limitations of the study

The study was an attempt to describe echocardiography alteration during physical stress exercise in healthy volunteers. An important limitation of this study is the low number of volunteers and the fact that volunteers of middle and older age are underrepresented or missing. It is also possible that differences of parameters at rest between genders were caused by the small account of volunteers in this pilot study (e.g. atrial flow velocities, iso-volumetric relaxation time, vena cava inferior diameter and diastolic blood pressure). As an attempt to reduce this disadvantage we created a correlation between tissue Doppler values and workload.

A second limitation is the fact that this study had only one single observer. So we could not describe an inter-observer variability. To reduce this disadvantage, we calculated the TDI values from those sides of the left ventricle with the well-known lowest inter-observer variation at rest and during exercise (10, 38). We also collected several cardiac cycles and calculated the mean values afterwards. We are sure that future studies will clarify these remaining questions.

### Conclusion

Stress echocardiography is a highly cost-effective method, easy to implement and widely available. Systolic and diastolic parameters of the left and right heart changed during exercise in relation to workload, but the estimated diastolic filling pressure and the pulmonary pressure stayed in a normal range.

Larger studies in the future have to analyze the impact of these values for patients with obvious left and/or right heart failure or in an early stage of such diseases.

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*Correspondence address*

Stefan A. Lange, M.D.  
Medizinische Klinik I  
Kardiologie und Internistische Intensiv-  
medizin  
Asklepios Harzlinik Goslar  
Kösliner Str. 12  
38642 Goslar  
Germany  
StefanAndreas.Lange@googlemail.com