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Left ventricular diastolic function is enhanced after peak exercise in endurance-trained adolescents as well as in their non-trained controls

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Summary

The aims of the study were to explore the temporal change of cardiac function after peak exercise in adolescents, and to investigate how these functional changes relate to maximal oxygen uptake ($\text{VO}_{2\text{max}}$).

The cohort consisted of 27 endurance-trained adolescents aged 13-19 years, and 27 controls individually matched by age and gender. Standard echocardiography and colour tissue Doppler were performed at rest, and immediately after as well as 15 minutes after a maximal cardio pulmonary exercise test (CPET) on a treadmill. The changes in systolic and diastolic parameters after exercise compared to baseline were similar in both groups. The septal E/e' -ratio increased immediately after exercise in both the active and the control groups (from 9.2 to 11.0; $p<0.001$, and from 8.7 to 10.2; $p=0.008$, respectively). In a comparison between the two groups after CPET, the septal E/e' -ratio was higher in the active group both immediately after exercise and 15 min later compared to the control group ($p=0.007$ and $p=0.006$, respectively). We demonstrated a positive correlation between $\text{VO}_{2\text{max}}$ and cardiac function including LVEF and E/e' immediately after CPET, but the strongest correlation was found between $\text{VO}_{2\text{max}}$ and LVEDV ($r=0.67$, $p<0.001$) as well as septal E/e' ($r=0.34$, $p=0.013$).

Enhanced diastolic function was found in both groups, but this was more pronounced in active adolescents. The cardiac functional response to exercise, in terms of LVEF and E/e' , correlates with the increase in VO_2 uptake. These findings in trained as well as untrained teenagers have practical implications when assessing cardiac function.

Keywords

Heart

Echocardiography

Training

Systolic function

Diastolic function

E/e'

Youngster

Introduction

Little is known about the normal response of the growing heart in well-trained as well as in untrained adolescents. Echocardiography provides useful insights into systolic function evaluated by using multiple parameters including ejection fraction (EF), fractional area change (FAC), mitral and tricuspid annular plane systolic excursion (MAPSE and TAPSE respectively), myocardial peak systolic velocity (s'), strain, and strain rate (Lang, *et al.*, 2015). Left ventricular (LV) diastolic function is assessed primarily on annular e' velocity, E/e' ratio, left atria (LA) maximum volume index, and peak tricuspid regurgitation (Nagueh, *et al.*, 2016).

The ratio of early diastolic mitral flow velocity to early diastolic velocity of the mitral annulus (E/e'), obtained by echocardiography both at rest and during exercise, has been shown to correlate with LV filling pressure and is therefore a parameter presently promoted for the non-invasive assessment of diastolic function (Burgess, *et al.*, 2006; Ommen, *et al.*, 2000). During exercise, ventricular filling time is reduced due to the higher heart rate (HR), thus the ability to increase LV inflow is of importance to enable a larger stroke volume without further increase in filling pressure (Nagueh, *et al.*, 2016; Sundstedt, *et al.*, 2007). An improved diastolic capacity in response to exercise may therefore be crucial in endurance trained subjects. In healthy children and adults (both athletes and non-athletes), increased mitral E as well as mitral annular e' velocities have been demonstrated at peak exercise, but data about the E/e' -ratio are somewhat conflicting. Some previous studies found an unaffected E/e' -ratio during and after exercise compared to the resting state (Neilan, *et al.*, 2006; Punu, *et al.*, 2012; Rowland, *et al.*, 2006; Santoro, *et al.*, 2015), while others reported an elevated E/e' -ratio, but still within normal limits (Cifra, *et al.*, 2016; Studer Bruengger, *et al.*, 2014). The only study that compares athletes with non-athletes was derived from an adult population (Studer

Bruengger, *et al.*, 2014), while comparisons between endurance-trained athletic and non-athletic adolescents are lacking. Also, data on temporal cardiac changes in association with maximal exercise are sparse.

If diastolic performance may be enhanced during exercise, such echocardiographic parameters at peak exercise would be associated with maximal oxygen uptake ($\text{VO}_{2\text{max}}$).

In a study on adults, $\text{VO}_{2\text{max}}$ to some extent correlated with enhanced exertional early diastolic mitral velocities at peak exercise, but $\text{VO}_{2\text{max}}$ correlated more consistently and higher with cardiac structural adaptation (Studer Bruengger, *et al.*, 2014).

The aims of the present study were to (i) investigate the extent and the temporal development of systolic and diastolic functional changes associated with a maximal exercise test in endurance-trained adolescents compared with an age- and gender-matched control group, and (ii) explore how parameters of cardiac function immediately after peak exercise relate to $\text{VO}_{2\text{max}}$ in the same subjects.

Methods

Study design and subjects

This prospective study, which is part of the Exercise Project at Jönköping University, Sweden, used a comparative and experimental pretest-posttest design with two individually age- and gender-matched groups consisting of in total 22 girls and 32 boys between 13-19 years of age. The endurance-trained subjects that comprised the active group were recruited from teams participating in orienteering and cross-country skiing in an area of southern Sweden, and the controls came from public schools within the same area. Inclusion criteria for the active group was endurance exercise at least 5 times a week, with training sessions of at least 30 min duration, for the previous 2 years or longer. The control group consisted of adolescents who did not exercise regularly. This amount of physical activity was in addition to taking part in mandatory physical education at school. All subjects were instructed to refrain from exercise on the day the test was performed. They also completed a questionnaire regarding exercise habits and medical conditions.

Written informed consent was obtained from all subjects, and the study was approved by the Regional Ethical Review Board in Linköping, Sweden (Dnr 2013/89-31). The study was executed in accordance with the Declaration of Helsinki.

Cardiopulmonary exercise test

Cardiopulmonary exercise test (CPET) was used to perform a maximal exercise session and to assess the $\text{VO}_{2\text{max}}$. All subjects exercised on a treadmill (RL2500E; Rodby, Vänge, Sweden) according to the modified Bruce protocol (Bruce, *et al.*, 1973). Breath-by-breath analysis of the volumes and concentration of exhaled O_2 and CO_2 was

performed using Jaeger Oxycon Pro (Vyair Medical, Danderyd, Sweden). Maximal VO_2 was averaged from the two highest, consecutive measurements immediately before exercise was terminated. Criteria for termination of exercise were exhaustion and/or a respiratory exchange ratio equal to or exceeding 1.1. Before the CPET, a resting 12-lead electrocardiogram (ECG) was recorded with the MAC 5500HD version 10 (GE Healthcare, Milwaukee, WI, USA), and right arm brachial artery systolic and diastolic blood pressure was obtained with the subjects in a supine position after at least 5 min of rest.

Echocardiography and image analysis

Echocardiographic examinations were carried out at three time-points for each participant; at rest before the CPET (baseline); within 1-2min after the CPET; and finally, 15min after the CPET. A state of the art ultrasound scanner (Vivid E9, GE Healthcare, Horten, Norway) equipped with an M5S probe was used. Offline analysis of echocardiographic data was performed by a single operator using EchoPAC PC version 110.0 (GE Healthcare, Horten, Norway).

Two-dimensional (2D) echocardiographic images were acquired from the parasternal long- and short-axis views, as well as from the apical long-axis ('three-chamber'), and two- and four-chamber views at a frame rate of > 40 frames/s. In addition to the standard four-chamber view, another clip was taken with focus on the RV. LV end-diastolic (LVEDV) and LV end-systolic volumes (LVESV), as well as LV ejection fraction (LVEF), was calculated with the biplane disk summation technique (Lang, *et al.*, 2015). LV peak global longitudinal strain (LVGLS) as well as LV strain rate were measured from the three standard apical views and averaged from 18 segments (six in each level,

base-mid-apex), using speckle tracking. The speckle-tracking region of interest (ROI) was adjusted to cover the entire wall thickness from the endocardial to the epicardial border. Measurements were accepted according to quality control included in the software. RV fractional area change (FAC), and RV longitudinal strain as well as RV strain rate of the free RV wall, were also evaluated. LA volume was calculated by the biplane method of disks (Lang, *et al.*, 2015). Total LA strain was assessed in the four-chamber LA-view, with the beginning of the P-wave as the reference point (Saraiva, *et al.*, 2010). Pulsed Doppler was used to obtain diastolic flow velocity across the mitral valve, specified as peak early diastolic (E) and late diastolic (A) flow velocities, at the tip of the mitral leaflets in the apical view. Notably, the E/A-ratio was not available in many of the subjects immediately after nor 15 minutes after the CPET, because of fusion of the E and A waves at the highest HR.

Colour tissue Doppler imaging loops were obtained in the apical two- and four-chamber views with a frame rate of > 100 frames/s. Peak systolic velocity (s') as well as early diastolic (e') and late diastolic (a') annular velocities were acquired from the base of the ventricle (septum-, lateral-, anterior-, and posterior walls). MAPSE and TAPSE were measured with the tissue tracking (TT) algorithm; i.e., s' measured by colour tissue Doppler integrated over time (Brodin, *et al.*, 1998). MAPSE was calculated by averaging the total amplitude measured from three consecutive heartbeats at the septal, lateral, inferior, and anterior aspects of the mitral annulus in the two- and four-chamber views. TAPSE, however, was obtained only from the lateral aspect of the tricuspid annulus in the four-chamber view focused on the RV.

Body surface area (BSA) was used to index the measurements of LV volumes, MAPSE, and TAPSE, respectively.

Statistics

Variables are presented as median value and range, or as number and percentage.

Because of non-normal distribution of the data, differences between the active group and controls were tested with the non-parametric Wilcoxon signed-rank test. To evaluate $\text{VO}_{2\text{max}}$ with the strongest associated functional parameters measured immediately after peak exercise, a multiple linear regression was used, and the analysis was performed in different steps. Multiple imputation was used for the missing data in correlation and regression analyses. One imputed variable was applied for E/e' lat, E/e' sept, mitral E, and RVFAC respectively. For LA volume index and RV e', the imputed variables were 15 and 10 respectively. Analysis weights were used in summaries of imputed values. A probability level of < 0.05 was considered significant. All statistics were performed with SPSS Statistics software version 21 (IBM software, Armonk, New York, USA).

Results

Except for higher $\text{VO}_{2\text{max}}$, and lower resting HR in the active group, there were no differences between the groups regarding demographic characteristics (Table 1). All subjects had a normal resting ECG, none of them reported a history of cardiovascular disease or smoking, and the only medical treatment reported was the regular use of bronchodilators to combat asthma in six active and one control, respectively. Image quality was excellent in all recorded loops. LV and RV strain, strain rate, and s' as well as LV volumes were visualized adequately in all subjects at all measurement times. The E/e'-ratio was possible to measure in 98% of the subjects at rest, 97% immediately after CPET, and 98% 15 minutes after CPET. Tissue velocity a' at the lateral and septal walls was measured in 96% of the participants, and a' at the free RV wall was quantified in 81%. RVFAC was obtained in 98% of the subjects.

Cardiac response to a maximal exercise test compared to baseline

Both groups responded to exercise with increased HR, and lowered LVESV. The LV systolic echocardiographic parameters, shown in Table 2, displayed similar changes in both groups, namely increases in LVEF, LVGLS and LV strain rate, as well as higher LV s' in both the septal and lateral walls. After 15 minutes of rest, the increase in LV systolic parameters including LV strain and MAPSE had disappeared and even lower values than at baseline were attained in either group (Table 2).

Diastolic echocardiographic parameters of the LV are presented in Table 3 and Figure 1. Mitral E, and LV a' at the septal wall were higher in both groups after peak exercise, whereas the LV a' at the lateral wall was increased only in the active group. Septal and lateral e' were all unchanged. The E/e'-ratio was higher immediately after exercise in

both groups, and an increase in LA total strain was also detected. Fifteen minutes after maximal exercise LV e' decreased compared to baseline in both septal and lateral walls, for both groups. Further, the E/ e' -ratio was still higher compared to baseline in the active group, but unchanged in the controls. At the same time after exercise, the E/ e' -ratio was higher in the active group both immediately after CPET and 15min later compared with the controls. LV a' at the lateral wall was decreased after 15 minutes of rest compared to baseline, which was more pronounced in the controls.

Increased RV strain rate and RVFAC were shown in both groups immediately post exercise (Table 4). However, increases in RV s' and TAPSE were found in the control group exclusively, while the active group had unchanged values of these parameters. Also, a' at the RV free wall was increased post exercise in both groups.

The following parameters were affected immediately after exercise in both groups and then returned to baseline after 15 minutes of rest: LVESV, LVEF, LV and RV strain rate, RVFAC, mitral E, LV a' at the septal wall, and LA total strain.

Association between maximal oxygen uptake and functional parameters measured immediately after exercise

The correlation between VO_{2max} and cardiac parameters measured immediately after peak exercise are summarized in Table 5. LVESV and lateral E/ e' were strongly correlated to LVEDV ($r = 0.8$) and septal E/ e' ($r = 0.75$) respectively and were therefore excluded in the step analysis. LVEDV indexed to BSA, and septal E/ e' were the strongest predictors of VO_{2max} . Also, LVEF and LA volume indexed to BSA correlated significantly to VO_{2max} , but these associations were weaker than LV volume and E/ e' .

Discussion

To our knowledge, this is the first study with focus on the cardiac changes from rest to maximal exercise in endurance-trained adolescents compared to a non-trained control group. We found similar responses to exercise in systolic and diastolic parameters in general for both the active and the control groups. That may indicate that the functional response to a short exercise session not is dependent on the degree of endurance training. Recently, we demonstrated considerable cardiac structural remodelling at rest in endurance trained adolescents compared to controls (Rundqvist, *et al.*, 2016), suggesting that long-term effects of regular exercise obviously affect cardiac morphology to a higher extent than cardiac function.

Systolic parameters of LV function such as LVEF, LVGLS, LV strain rate, and septal and lateral LV s', were all increased immediately after exercise in both groups compared to baseline, which is consistent with previous studies in both adults and a healthy pediatric cohort (Cifra, *et al.*, 2016; La Gerche, *et al.*, 2012), indicating an increased myocardial contractility. Furthermore, we found lower values of MAPSE and LVGLS in both groups 15 minutes after end of exercise compared to baseline. These reductions most probably reflect decreased stroke volume and changes in loading conditions at this later stage, which is consistent with a previous study on physically active adolescents at 30 minutes following exercise (Fomin, *et al.*, 2014). Fomin et al also showed that LV myocardial responses to maximal exercise did not differ between male and female subjects. We could not, however, perform subgroup analyses of gender due to the relatively small sample size.

Regarding LV diastolic parameters, we found increased mitral E immediately after peak exercise in both groups, which previously has been shown in both adults and adolescents

(Cifra, *et al.*, 2016; La Gerche, *et al.*, 2012; Santoro, *et al.*, 2015; Studer Bruengger, *et al.*, 2014). This could be due to a remaining elevation in stroke volume which has to be accommodated by an increase in LV filling. This is in line with the increase in LA total strain and LV a' immediately after exercise which suggests that atrial function is enhanced and important in the response to exercise. We have not found any previous reports on LA strain in response to an exercise challenge.

Further, we confirmed that exercise-induced E/e' enhancement is not unique to endurance-trained adolescents, since similar patterns were found in both groups. It has previously been reported that increased E/e' as seen in adult athletes reflected higher atrial filling pressures and higher LA volume which may contribute to atrial remodelling over time and thus also increase the risk of atrial fibrillation (Stumpf, *et al.*, 2016).

Mutual comparison between the groups in our study showed that the active group had higher E/e' both immediately as well as 15 minutes after ended exercise compared with the controls. In addition, increased E/e' levels were still elevated 15 minutes after exercise compared to baseline in the active group, unlike for the controls who then had returned to baseline levels. These findings indicate a probable adaptation in diastolic filling pressure, i.e. the diastolic function, after a short maximal exercise session, which was more obvious in endurance-trained adolescents than in the control group. Our results demonstrating increased E/e' are consistent with a previous study on adults aged < 40 years, (Studer Bruengger, *et al.*, 2014), and another study on healthy children and adolescents (Cifra, *et al.*, 2016). The former, however, did not record any difference between the groups of athletes and non-athletes in E/e' at peak exercise as we did, and the latter did not separate E/e' into septal and lateral wall nor divide the subjects into groups according to the degree of exercise history. Our results contradict another study on youngsters where the E/e' ratio remained unaltered with exercise (Punn, *et al.*, 2012).

However, in that study E/e' was measured at a peak HR of 160 beats/min for all participants which may not be the level of maximal HR in a younger population. Fifteen minutes after peak exercise we demonstrated that the levels of LV e' at the septal and lateral walls were lower than at baseline in both groups, which was not detected immediately after exercise. This delayed effect may indicate attenuated LV diastolic function in the recovery phase following exercise (Fomin, *et al.*, 2014).

Immediately after exercise, RV strain rate and RVFAC were increased in both groups compared to baseline. Further, TAPSE and s' of the free RV wall were increased in the controls, not in the active group. This finding is in contrast to several previous studies on adult athletes that have demonstrated cardiac dysfunction associated with exercise exertion, especially for the RV (La Gerche, *et al.*, 2012; Neilan, *et al.*, 2006; Oxborough, *et al.*, 2011; Trivax, *et al.*, 2010). These previous studies, however, were performed on athletes who had completed a marathon race or another type of ultradistance-race, which is in contrast with our study that exerted a maximum effort by a short maximal exercise test. D'Andrea *et al.* declared in their main topic (D'Andrea, *et al.*, 2015) that the magnitude of the effect on ventricular function seemed to be related to both intensity and duration of exercise. They further proposed that the RV seems to be capable to meet the work requirements of short bouts of intense exercise, while prolonged exercise can induce cardiac “fatigue” where the RV could be more susceptible than LV. In addition, previous studies on cardiac function after a short intense maximal test, such as our test, are consistent with our results of increased post-CPET systolic and diastolic parameters (Cifra, *et al.*, 2016; Rowland, *et al.*, 2006; Studer Bruengger, *et al.*, 2014). This may contribute to the various results in studies of cardiac function in response to exercise in endurance athletes. RV strain tended to be lower in the active group 15 minutes after peak exercise indicating a delayed reduction of RV strain. This observation has been

demonstrated in a previous study of athletes within an hour after an ultramarathon (Oxborough, *et al.*, 2011), however, studies of temporal changes close to an exercise session are rare.

In our earlier study, we found a strong correlation between $\text{VO}_{2\text{max}}$ and resting cardiac dimensions, and an additionally but weaker correlation to resting RV function (Rundqvist, *et al.*, 2016). In our present study, where we assessed the correlation of $\text{VO}_{2\text{max}}$ and cardiac parameters immediately after a short maximal exercise test, we demonstrate that LA volume and systolic function such as LVEF were positively correlated to $\text{VO}_{2\text{max}}$, but the strongest correlation to $\text{VO}_{2\text{max}}$ was found in LV volume and E/e' . These data indicate that much of the variation in $\text{VO}_{2\text{max}}$ is explained by a combination of increased cardiac dimensions (predominantly LV) and filling pressure. Previous studies on adults performed at rest and during exercise have shown that LV volume is of importance for $\text{VO}_{2\text{max}}$ (La Gerche, *et al.*, 2012; Studer Bruengger, *et al.*, 2014). An earlier study in the elderly has demonstrated that LV filling did not enhance during exercise, irrespective of lifelong exercise frequency, and further, that an improved regulation of stroke volume was not connected to favourable effects on LV filling during exercise (Hummel, *et al.*, 2012). To our knowledge, however, there are no studies in healthy adolescents and adults on the correlation of $\text{VO}_{2\text{max}}$, LA volume and filling pressure close to maximal exercise.

Body size may have differed between the active group and controls, therefore individual matching for age and gender was undertaken to control for these variances. Additionally, BSA did not differ between the groups. All echocardiographic measurements were obtained in a supine position which implies higher cardiac preload compared to studies that analysed cardiac function during an upright cycle test or with the subjects in a

semisupine position. This study evaluated endurance trained adolescents, therefore our findings may not be applied to other sports.

In conclusion, our findings show that increased cardiac requirements during exercise in adolescents are met with both systolic and diastolic improvement of various aspects of LV function, regardless of exercise history. Systolic function improved in terms of higher LVEF, LV strain, LV strain rate, and LV s' in both the active and in the control groups. Additionally, enhanced diastolic function was found in terms of increased mitral E, E/e'-ratio, LV a', and LA strain in both groups, but was more pronounced in the active group. However, the RV response to exercise was of a lower magnitude than that of the LV. However, systolic RVFAC, RV strain rate, and a diastolic RV a' increased in both groups.

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Conflict of interest: none declared.

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Table 1. Demographic data and general physical characteristics of the study population

	Active group (n=27)	Controls (n=27)	P value
Girls	11 (41%)	11 (41%)	1.0
Age (years)	15.5 (13–19)	15.4 (13–19)	0.95
BSA (m ²)	1.66 (1.37–1.98)	1.72 (1.26–2.23)	0.48
Resting SBP (mmHg)	120 (95–155)	115 (105–130)	0.31
Resting DBP (mmHg)	65 (55–80)	65 (50–85)	0.52
HR at rest (beats/min)	63 (42–85)	71 (49–88)	0.013
HR max (beats/min)	195 (180–214)	196 (175–208)	0.86
HR 1–2min post exercise (beats/min)	125 (94–153)	127 (102–155)	0.86
HR 15min post exercise (beats/min)	94 (80–109)	97 (71–122)	0.43
VO _{2max} (mL/kg/min)	62 (52–79)	43 (27–62)	<0.001

Data are expressed as number (percentage) or as median (range). Bold styling denotes statistical significance. BSA, body surface area; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; VO_{2max}, maximal oxygen uptake.

Table 2. LV and LA dimensions, and LV systolic echocardiographic parameters at baseline and post exercise, in the active group (a) vs. controls (c)

		Baseline, pre exercise	1-2min post exercise	p-value*	15min post exercise	p-value*
LVEDVind (mL/m ²)	a	60 (50–80)**	60 (51–85)**	0.866	60 (47–78)**	0.093
	c	50 (38–72)	52 (40–69)	0.414	47 (33–68)	0.061
LVESVind (mL/ m ²)	a	24 (18–31)**	16 (11–29)	<0.001	23 (16–38)**	0.755
	c	20 (15–29)	14 (11–19)	<0.001	19 (12–30)	0.079
LV length	a	8.4 (6.9–10.0)**	8.1 (7.1–9.4)	0.009	8.1 (6.8–9.5)	0.017
	c	7.8 (6.0–9.5)	7.7 (6.4–9.4)	0.607	7.7 (6.1–9.6)	0.288
LA volume index	a	27 (21–36)**	17 (10–23)**	<0.001	16 (9–26)**	<0.001
	c	19 (14–31)	12 (9–21)	<0.001	13 (8–19)	<0.001
LV stroke volume (ml)	a	58 (50–94)**	69 (58–117)**	<0.001	59 (44–94)**	0.011
	c	48 (33–87)	61 (40–101)	<0.001	48 (31–83)	0.093
LVEF (%)	a	61 (57–67)	73 (66–79)**	<0.001	59 (52–67)	0.102
	c	59 (54–67)	72 (69–77)	<0.001	60 (55–70)	0.428
LVGLS (%)	a	22 (19–25)	24 (20–27)	0.001	20 (16–23)	<0.001
	c	21 (19–27)	24 (18–29)	0.015	20 (15–26)	<0.001
LV strain rate (s ⁻¹)	a	1.2 (1.0–1.6)	2.0 (1.5–2.8)	<0.001	1.3 (1.0–1.6)	0.092
	c	1.3 (1.0–1.6)	2.2 (1.5–2.7)	<0.001	1.4 (1.1–2.1)	0.015
LV s' sept (cm/s)	a	6.7 (5.1–8.7)	9.0 (5.4–11.7)	<0.001	6.9 (5.1–8.9)	0.589
	c	6.7 (5.0–9.7)	9.0 (6.9–13.5)	<0.001	7.0 (5.5–9.6)	0.509
LV s' lat (cm/s)	a	7.9 (5.0–11.8)	10.8 (6.9–17.9)	<0.001	8.6 (5.1–15.5)	0.032
	c	8.7 (6.3–12.6)	11.6 (6.6–18.3)	<0.001	9.0 (6.9–13.9)	0.302
MAPSEind (mm/m ²)	a	8.3 (6.2–10.7)	8.8 (6.6–10.8)	0.203	7.7 (6.1–9.0)	<0.001
	c	8.4 (5.6–10.8)	8.5 (6.6–12.0)	0.002	7.4 (5.8–9.6)	<0.001

Data presented as median with the range in parenthesis. Bold styling denotes statistical significance. *against baseline. ** significance <0.05 between the groups at a given time point. LVEDVind and LVESVind, left ventricular end diastolic and systolic volume indexed by Body Surface Area; LVEF, left ventricular ejection fraction; LVGLS, left ventricular global longitudinal strain; s', peak systolic velocity; MAPSE, mitral annular plane systolic excursion indexed by BSA.

Table 3. LV diastolic echocardiographic parameters at baseline and post exercise, in the active group (a) vs. controls (c)

		Baseline, pre exercise	1-2min post exercise	p-value*	15min post exercise	p-value*
Mitral E (cm/s)	a	102 (76–125)	122 (90–159)	<0.001	100 (75–124)**	0.195
	c	96 (72–117)	115 (75–154)	0.001	88 (66–121)	0.062
LV e' sept (cm/s)	a	11 (8–15)	11 (7–16)	0.517	9 (5–15)	0.001
	c	11 (8–13)	11 (9–15)	0.055	10 (6–14)	0.015
LV e' lat (cm/s)	a	16 (11–21)	15 (9–20)	0.564	13 (6–19)	<0.001
	c	15 (10–20)	16 (9–22)	0.387	13 (8–18)	0.001
LV a' sept (cm/s)	a	4.6 (1.8–7.7)	6.8 (3.4–13.4)	<0.001	4.4 (2.0–8.0)**	0.904
	c	5.1 (3.2–8.1)	7.5 (3.9–13.9)	<0.001	5.3 (3.5–9.3)	0.209
LV a' lat (cm/s)	a	4.1 (2.0–6.4)	5.7 (2.4–10.1)	<0.001	3.2 (1.5–6.3)	0.648
	c	4.4 (2.5–7.1)	4.9 (2.6–7.6)	0.143	3.5 (1.9–11.4)	0.019
E/e'- ratio sept	a	9.2 (6.6–13.6)	11.0 (8.1–22.9)**	<0.001	10.4 (7.4–16.2)**	0.006
	c	8.7 (5.8–12.3)	10.2 (6.0–13.1)	0.008	9.0 (6.7–11.8)	0.517
E/e'- ratio lat	a	6.4 (4.8–9.5)	8.0 (5.8–18.0)	<0.001	7.4 (4.6–14.6)	0.001
	c	6.4 (4.5–9.3)	7.3 (4.3–12.1)	0.002	6.7 (5.4–9.4)	0.073
LA total strain (%)	a	39 (31–53)	45 (37–61)	0.001	36 (28–53)	0.361
	c	38 (28–52)	43 (27–96)	0.034	37 (28–53)	0.819

Data presented as median with the range in parenthesis. Bold styling denotes statistical significance. *against baseline. ** significance <0.05 between the groups at a given time point. E, early mitral inflow velocity; e', early peak tissue velocity; a' late diastolic peak tissue velocity; LA, left atrium.

Table 4. RV systolic and diastolic echocardiographic parameters at baseline and post exercise, in the active group (a) vs. controls (c)

		Baseline, pre exercise	1-2min post exercise	p-value*	15min post exercise	p-value*
RV strain (%)	a	27 (19–34)	23 (16–35)	0.923	23 (12–33)	0.055
	c	28 (19–33)	28 (16–41)	0.919	26 (7–39)	0.349
RV strain rate (s ⁻¹)	a	1.4 (1.0–2.2)	2.2 (1.5–3.3)	<0.001	1.4 (0.8–2.6)	0.421
	c	1.5 (1.1–2.4)	2.4 (1.4–3.4)	<0.001	1.6 (1.0–2.7)	0.819
RV s' (cm/s)	a	11.2 (7.3–14.6)**	11.8 (7.3–17.8)	0.124	10.0 (6.5–12.8)	<0.001
	c	10.0 (7.8–14.1)	12.5 (7.3–17.2)	<0.001	10.1 (5.6–14.7)	0.829
TAPSEind (mm/m ²)	a	12 (7–16)**	12 (7–15)	0.532	11 (8–15)	0.019
	c	10 (8–17)	11 (7–18)	0.002	10 (7–17)	0.866
RVFAC (%)	a	42 (36–49)	58 (41–69)	<0.001	42 (32–57)	0.694
	c	41 (35–48)	56 (43–66)	<0.001	42 (24–56)	0.061
RV e' (cm/s)	a	11 (7–16)	11 (5–14)**	0.115	10 (5–18)	0.114
	c	11 (8–15)	12 (7–20)	0.058	10 (7–17)	0.811
RV a' (cm/s)	a	6.3 (3.4–10.6)	12.2 (5.1–25.1)	<0.001	7.5 (2.5–19.8)	0.159
	c	5.3 (2.3–10.2)	13.8 (2.6–27.1)	<0.001	7.9 (2.6–23.8)	0.023

Data presented as median with the range in parenthesis. Bold styling denotes statistical significance. *against baseline. ** significance <0.05 between the groups at a given time point. RV, right ventricle; s', peak systolic velocity; TAPSEind, tricuspid annular plane systolic excursion indexed by Body Surface Area; RVFAC, right ventricular fractional area change; e', early peak tissue velocity; a' late diastolic peak tissue velocity.

Table 5. Correlations and multiple linear regressions in steps of cardiac variables 1-2min post exercise vs. maximal oxygen uptake mL/kg/min.

Correlation			Linear regression					
			Step 1		Step 2		The final model*	
	r	p-value	Beta	p-value	Beta	p-value	Beta	p-value
LVESVind	0.39	0.004						
LVEDVind	0.67	<0.001	0.71	<0.001			0.74	<0.001
LVEF	0.41	0.002	1.08	0.014			0.45	0.331
LV s' sept	0.09	0.513						
LV s' lat	0.15	0.282						
LV e' sept	0.16	0.236						
LV e' lat	0.13	0.354						
LV E/e' lat	0.31	0.024						
LV E/e' sept	0.34	0.013			1.75	0.016	1.32	0.005
LA volume index	0.35	0.010			0.70	0.034	0.16	0.465
Mitral E	0.27	0.051			-0.07	0.546		
RVFAC	0.02	0.912						
RV s'	0.09	0.500						
RV e'	0.19	0.159						

Bold styling denotes statistical significance. For abbreviations, see previous tables. *The final model includes variables that had $p < 0.05$ at step 1 and 2.

Figure 1. Mean E/e' (septal and lateral walls) recorded in the active and in the control groups at baseline (rest), and 1-2 min as well as 15 min after peak exercise respectively. * $p < 0.01$ for the difference between active and control group; + $p < 0.001$ for the difference between baseline and post exercise in active group; o $p < 0.01$ for the difference between baseline and post exercise in control group.