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**Determinants of kinetic energy of blood flow in the four-chambered
heart in athletes and sedentary controls**

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Key words: diastolic function, atrium, ventricle, vortex formation,

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ABSTRACT

Background: Kinetic energy (KE) of intra-cardiac blood may play an important role in cardiac function. The aims of this study were 1) quantify and investigate determinants of KE, 2) compare KE expenditure of intra-cardiac blood between athletes and controls, 3) quantify the amount of KE inside and outside the diastolic vortex.

Methods: 14 athletes and 14 volunteers underwent cardiac magnetic resonance imaging including 4-dimensional phase-contrast sequences. KE was quantified in 4 chambers and energy expenditure was calculated by determining mean KE/cardiac index.

Results: Left ventricular (LV) mass was an independent predictor of diastolic LVKE ($R^2=0.66$, $p<0.001$) while right ventricular (RV) end-diastolic volume was important for diastolic RVKE ($R^2=0.76$, $p<0.001$). Mean KE/cardiac index did not differ between groups (controls 0.53 ± 0.14 , athletes $0.56\pm 0.21\text{mJ}/(\text{L}/\text{min}/\text{m}^2)$, $p=0.98$). Mean LV diastolic vortex KE made up $70\pm 1\%$ and $73\pm 2\%$ of total LV diastolic KE in athletes and controls ($p=0.18$).

Conclusion: The characteristics of the LV as a pressure pump and the RV as a volume pump are demonstrated as an association between LVKE and LV mass and between RVKE and end-diastolic volume. This also suggests different filling mechanisms where the LV is dependent on diastolic suction while the RV fills with a basal movement of the atrioventricular-plane over “stationary” blood. Both groups had similar energy expenditure for intra-cardiac blood flow indicating similar pumping efficiency, likely explained by the lower heart rate which cancels the higher KE per heart beat in athletes. The majority of LVKE is found within the LV diastolic vortex in contrast to earlier findings.

NEW AND NOTEWORTHY

In line with the different filling mechanisms for the ventricles it was shown that LVM is a determinant of kinetic energy for left ventricular filling whereas for the right ventricle EDV, i.e. blood mass, determines kinetic energy. Furthermore, 70% of diastolic kinetic energy is found inside the LV diastolic vortex.

BACKGROUND

The athlete's heart is characterized by increased volumes and mass (3, 17, 36) as well as improved diastolic (43) and systolic function (4, 8). These adaptations are necessary to supply muscles with oxygen during high intensity exercise. As described by Kilner et al. (25) the human heart is looped and therefore redirects blood through its curvatures with minimal dissipation of energy. In contrast to pathological enlargement of the heart, e.g. as seen in heart failure, the geometry of the heart is preserved when it adapts to long term endurance training (36). During exercise, the momentum of blood may gain functional importance (11, 25) and it can be hypothesized that athletes' hearts, which are adapted to pumping large blood volumes, have adapted to further improve the blood flow through the heart. The momentum of blood can be quantified as kinetic energy and there is an increasing number of publications on the topic using both echocardiography (1, 6, 26) and cardiovascular magnetic resonance imaging (CMR) (15, 29, 37, 45). Kinetic energy has been shown to differ between the left and right side of the heart (2, 11) but the determinants of kinetic energy remain to be elucidated.

The inflowing blood to the left ventricle during diastole forms a vortex (29) that has been connected to diastolic function and overall cardiac health (20, 21, 31). As suggested by Pedrizetti et al. (30), altered flow patterns such as in vortices could signal the presence of poor

cardiac function even before noticeable structural changes arises. Recently, a study used two-dimensional measurements of KE within the vortex in healthy and dilated hearts and found rather low KE within the vortex, although with a large range (6). As the intraventricular vortex has a complex three-dimensional shape (39) a three-dimensional technique may provide better quantifications of KE within and outside the vortex. Phase-contrast cardiac magnetic resonance (CMR) provides the ability to quantify time-resolved KE in three-dimensional space covering the entire heart.

The differences in velocity for filling and ejection of blood in athletes compared to controls likely leads to differences in kinetic energy of intra-cardiac blood flow ($KE = \frac{1}{2}mv^2$ where m is mass and v is velocity). For a given body size, metabolic demands at rest are similar between individuals and consequently cardiac index (CI) is approximately 3 l/min/m² in normal subjects as well as elite athletes (9). A large heart, as seen in endurance athletes, achieves this CI at lower heart rates and higher stroke volumes (SV) compared to smaller hearts. As the duration of systole remains fairly constant, athletes must eject a larger volume of blood at a given time, which is achieved by increasing the velocity of blood. During diastole the large heart fills with a larger volume at the same given time during the rapid filling phase, and once again this is achieved by increasing the velocity. Kinetic energy constitutes a small part of the total work performed by the heart at rest (28, 32), and is considered to increase during exercise (11). By calculating the energy expenditure as meanKE/CI, we can calculate how much KE is used to maintain an adequate CO at rest and provide a reference material for future measurements of KE during exercise.

Therefore, the aims of this study were to 1) quantify KE and investigate determinants of KE in the four chambers of the heart in highly trained endurance athletes and healthy controls, 2)

compare kinetic energy expenditure of intra-cardiac blood flow between these groups, and 3) quantify the amount of KE inside and outside the left ventricular diastolic vortex.

METHOD

The study follows the Declaration of Helsinki and ethical approval was given by the Ethical Review Board, Lund, Sweden. All participants provided written informed consent.

Study population and design

Fourteen elite endurance athletes (eight women) and 14 healthy sedentary or recreationally active volunteers (six women) underwent cardiac magnetic resonance imaging (CMR). A subgroup of the control population included in the present study has been used in two previous studies of 4D PC-MR (2, 11). To ensure high fitness level of the athletes, this group underwent maximal exercise testing on ergometer cycle (Monark 939 E, Vansbro, Sweden) to determine peak oxygen uptake (Oxycon Jaeger, Hochberg, Germany). All test subjects were non-smokers, presented with blood pressure $\leq 140/90$, normal ECG, no medication, and had no history of cardiovascular or systemic disease.

Cardiovascular magnetic resonance imaging

All healthy volunteers were assessed using a 3T scanner (Philips Medical System, Best, The Netherlands). All athletes were assessed using a 1.5T scanner and six healthy volunteers underwent a re-scan at 1.5T (Philips Medical System Best, The Netherlands). Images were acquired using sequences with identical temporal and spatial resolution at both field strengths, as previously described (2, 11). Validations of equivalence in 4D PC measures between scanners have previously been performed and published by our group (12, 23).

Image analysis

All measurements were done using the software Segment 1.9 (<http://segment.heiberg.se>) (22). Kinetic energy was calculated using an in-house developed module of the software. Before analyzing 4D PC data, a first-order polynomial fit was used to correct for eddy currents and other phase background effects. Furthermore, velocity aliasing was corrected using semi-automatic phase unwrapping. Kinetic energy was visualized in the long-axis and short-axis views using the open source flow visualization software FourFlow 1.2 (<http://fourflow.heiberg.se>).

Atrial and ventricular volumes

Atrial volumes were measured in short-axis images at the time of ventricular end-diastole and ventricular end-systole. Ventricular mass (LVM, RVM), end-diastolic volume (LVEDV, RVEDV), end-systolic volume (LVESV, RVESV) and stroke volume (LVSV, RVSV) were measured in short-axis images using manual delineations of endocardial (for volumes) and epicardial borders (for mass) of the ventricle. Papillary muscles were not included in LVM measurements. Peak filling rate (PFR) and peak ejection rate (PER) of the LV and RV were calculated as the derivatives of the steepest decreasing and increasing parts of the volume curves (27).

Total heart volume (THV) was measured in short-axis images by manual delineation and was defined as the volume of all structures within the pericardium as previously described (10).

Atrioventricular plane displacement

Atrioventricular plane displacement (AVPD) for the left and right ventricle was determined from CMR long-axis images as previously described (13, 14). In short, markers indicating the location of the atrioventricular plane were placed in the 2ch, 3ch and 4ch images at end

diastole and end systole and the distance travelled by the markers were used to calculate the AVPD. Longitudinal contribution to SV was calculated as $SV_{\text{long}} = \text{AVPD} * \text{ventricular short axis area}$ (14).

In vivo kinetic energy measurements

Kinetic energy peaks of both ventricles and atria are named after the ventricular phases in the cardiac cycle. Thus, although the atria fill when the ventricles eject, both the atrial and ventricular peaks at this time point will be referred to as systolic peaks. Consequently, diastolic peaks of the ventricle coincide with both decreasing atrial volume and contraction but peaks for both atria and ventricles are referred to as diastolic peaks.

In vivo KE was quantified as previously described (2, 11). In short, atrial and ventricular volumes were manually delineated in all slices and all timeframes in short-axis cine images. The delineations were thereafter transferred to the corresponding 4D PC image and manual corrections were made to ensure correct delineation of the blood volume. Blood mass was calculated by multiplying blood volume with density of blood, assumed to be 1.05g/cm^3 (40). Kinetic energy of each voxel was calculated as $KE = \frac{1}{2}mv^2$, where m is blood mass and v velocity of the blood. Total KE was calculated for each timeframe as the sum of KE in all voxels in the atria and ventricles, respectively.

Kinetic energy expenditure

Cardiac output is the amount of blood needed to meet the metabolic demand of the body. In this study, body surface area (BSA) varies widely and therefore cardiac index ($CI = CO/BSA$) was used as a measure of metabolic demand at rest as it takes differences in body size into

account. The amount of energy used to circulate enough blood to meet the metabolic demands over one minute at rest was therefore calculated as *mean KE / CI*.

Rotational kinetic energy of the atria

Rotational kinetic energy was calculated as previously described by Arvidsson et al. (2). In short, the atrial center of mass was first computed using delineations from 4D PC images. Angular momentum about the atrial center of mass was calculated using positional and velocity vectors for each individual voxel. Total angular momentum was then computed through summation of all voxels. The axis of rotation was determined using direction of angular momentum around the center of mass. Rotational KE (RKE) for each voxel was calculated as $RKE = \frac{1}{2}mv_{\alpha}^2$, where m is mass and v_{α} is the angular velocity around the rotational axis. Total RKE was calculated by summing all voxels for each atrium. To determine whether rotational flow was helical or non-helical during the early rapid filling phase, the angle between the rotational axis and the average flow direction was computed. Average flow direction was determined by the vector sum of the voxels in the atrial blood pool. Helical flow is indicated by values near 0 or 180 degrees, while values near 90 degrees indicate non-helical flow.

Vortex ring size and KE

To calculate vortex size, Lagrangian coherent structures (LCS) were computed from 4D PC data as previously described (39). Particle-tracing computations required for the LCS algorithm were performed on Graphical Processing Unit (GPU) cards implemented in CUDA-C. The LCS indicative of vortex-ring formation was manually delineated in long-axis views and used to guide delineation of vortex-ring volume in short-axis slices over time. Vortex

delineations were thereafter imported to the KE analysis dataset for calculations of KE inside of the vortex.

Kinetic energy validation

Kinetic energy measurements were validated using a previously described phantom setup (38). Velocities were measured in a phantom setup, consisting of a water tank for vortex ring generation, and a pulsatile pump. Five different pump settings were used, with stroke volumes ranging from 12 to 37 ml. Velocities were measured using 4D PC-MR and particle imaging velocimetry (PIV), a laser-based method for flow measurement. Experiments were carried out using water and a glycerine-water mixture to approximate the viscosity of blood. Axial symmetry of the vortex ring was assumed when quantifying KE.

To assess the effect of reduced temporal and spatial resolution on KE measurements, a downsampling analysis was performed by reducing the resolution in already acquired data. For the phantom experiments, one of the PIV velocity measurements was downsampled in time and space. The downsampling factors were 1, 3, 5, 7 and 9 in time and 1, 2, 3 and 4 in space. Smoothing filters were applied before decimation of the images by averaging neighbouring grid points in time and space. The number of neighbours used in the averaging in each direction was equal to the downsampling factor. Kinetic energy was then quantified using the downsampled velocity data. To assess the effect of resolution in vivo, 4D PC velocity data from one subject was downsampled by a factor 2 in time and a factor 2 in space separately.

Exercise testing

Athletes underwent maximal exercise testing on ergometer cycle with breath-by-breath measurements of oxygen uptake. Measurements of oxygen uptake were averaged over ten

seconds and peak oxygen uptake (VO_2peak) was calculated as the average of the three highest values during the last minute of exercise at a respiratory exchange ratio >1.15 .

Statistical analysis

Values used to describe characteristics of the study population are presented as mean \pm standard deviation (SD). Atrial and ventricular energy values are presented as mean \pm standard error of the mean (SEM). As normal distribution could not be assumed, Mann-Whitney non-parametric test was used to test for differences between groups. Differences between groups with a p-value <0.05 were considered statistically significant. To determine which factors are influencing diastolic KE in the different chambers a stepwise multiple linear regression analysis was performed. For the LV and RV, mass, stroke volume, end-diastolic volume and SV_{long} (ml) were used. To investigate what affects atrial filling, determinants of atrial systolic peak KE (systolic referring to the phase of the cardiac cycle held by the ventricle at this time point) were investigated using ventricular SV, peak ejection rate of the ventricle (PER), ventricular SV and SV_{long} (ml). Furthermore, a multiple regression analysis was performed for mean KE of the left and right ventricle, with SV, HR, RR-interval and BSA as independent variables.

RESULTS

Peak oxygen uptake in male athletes was $67\pm 3 \text{ ml min}^{-1} \text{ kg}^{-1}$ (63-72) and for female athletes $54\pm 4 \text{ ml min}^{-1} \text{ kg}^{-1}$ (47-59), thus confirming high fitness status. One athlete did not reach VO_2peak and is therefore excluded from all analyses where oxygen uptake is used. Subject characteristics and cardiac volumes are presented in Table 1.

Kinetic energy of the atria and ventricles

The peaks of LV and RV differ in amplitude and timing where the left atrium and ventricle both displayed the highest peak during early diastole while the right atrium and ventricle showed the highest peak during systole (Figure 1A-D). Mean KE for the LV and RV were strongly correlated ($R^2=0.88$, $p<0.0001$, Figure 2A). Furthermore, mean KE of the atria and ventricles over the cardiac cycle did not differ between athletes and controls (Table 2). Peak KE at early diastole in the left and right ventricle was higher in athletes compared to controls (8.9 ± 1.1 mJ vs 5.9 ± 0.4 mJ, $p=0.04$ for LV and 4.2 ± 0.5 mJ vs 3.1 ± 0.4 mJ, $p=0.03$ for RV). Also peak systolic KE of the LA was higher in athletes compared to controls (2.3 ± 0.3 mJ vs 1.4 ± 0.2 mJ, $p=0.006$). When normalizing mean KE for heart rate, only LAKE differed between groups (controls 0.017 ± 0.001 mJ/beat, athletes 0.25 ± 0.002 mJ/beat, $p=0.015$). Values for mean KE, systolic, early diastolic and late diastolic peak KE are presented in Table 2.

Peak oxygen uptake correlated to mean KE (LVKE $R^2=0.37$ $p<0.05$, RVKE $R^2=0.51$ $p<0.01$), to systolic peak KE (LVKE $R^2=0.41$ $p<0.05$, RVKE $R^2=0.58$ $p<0.01$) and to early diastolic peak KE (LV $R^2=0.72$, $p<0.0001$, RV $R^2=0.76$, $p<0.0001$). There was no correlation between late diastolic peak KE and VO_2 peak.

Determinants of kinetic energy

Univariate correlation between early diastolic peaks and mass, SV, EDV and SV_{long} (ml) for the left and right ventricles are presented in Table 3. Left ventricular mass was an independent predictor of LV early diastolic peak KE ($R^2=0.66$, $p<0.001$). Inclusion of LVSV, LVEDV and $LVSV_{long}$ (ml) did not add to the model (Table 3). For RV early diastolic peak KE, RVEDV

was an independent predictor ($R^2=0.76$, $p<0.0001$). Adding and $RVS_{V_{long}}$ (ml) to the model further increased the predictive value ($R^2=0.80$, $p=0.042$) (Table 3).

As atrial filling occurs during ventricular systole when the AV-plane moves towards the apex, the determinants of the peaks during ventricular systole were used to assess determinants of atrial filling. Left ventricular SV was an independent predictor of KE of the left atrium during ventricular systole ($R^2=0.39$, $p<0.0001$) (Table 4). Right ventricular $SV_{long(ml)}$ was an independent predictor of KE of the right atrium during ventricular systole ($R^2=0.56$, $p<0.0001$) and RV PER further increased the predictive value ($R^2=0.63$, $p=0.042$) (Table 4).

Mean LVKE was associated with LVSV ($R^2=0.48$, $p<0.0001$) and HR added further to the predictive value ($R^2=0.60$, $\beta=0.73$ for SV and $\beta=0.35$ for HR, $p<0.0001$). Similarly, mean RVKE was associated with RSV ($R^2=0.64$, $p<0.0001$) and HR added further to the predictive value ($R^2=0.80$, $\beta=0.86$ for SV and $\beta=0.41$ for HR, $p<0.0001$).

Energy expenditure per blood volume

Right atrial kinetic energy normalized for SV (RAKE/RSV) was higher in controls (16 ± 3 vs 13 ± 4 $\mu\text{J}/\text{ml}$, $p=0.04$), while there was no difference between groups for LAKE/LVSV, RVKE/RSV or LVKE/LVSV (Figure 3). The amount of KE needed to meet the metabolic demands at rest, measured as mean LVKE/CI did not differ between athletes and controls (0.56 ± 0.06 and 0.53 ± 0.04 $\text{mJ}/(\text{l}/\text{min}/\text{m}^2)$, $p=0.98$). Furthermore, there were no differences between groups when comparing RVKE/CI (0.62 ± 0.0 and 0.58 ± 0.04 $\text{mJ}/(\text{l}/\text{min}/\text{m}^2)$, $p=0.95$), LAKE/CI (0.30 ± 0.03 and 0.30 ± 0.02 $\text{mJ}/(\text{l}/\text{min}/\text{m}^2)$, $p=0.45$) or RAKE/CI (0.46 ± 0.04 and 0.51 ± 0.04 $\text{mJ}/(\text{l}/\text{min}/\text{m}^2)$, $p=0.35$). Furthermore, there was no difference between groups for

mean LVKE/CO (0.32 ± 0.02 and 0.27 ± 0.02 mJ/l/min, $p=0.21$), or mean LVKE/(SV/BSA) (0.033 ± 0.003 mJ/ml/m² for controls and 0.029 ± 0.003 for athletes, $p=0.19$) (Figure 4).

Kinetic energy inside and outside the vortex

Mean KE of the diastolic vortex contributed $70\pm 1\%$ and $73\pm 2\%$ of LV total diastolic KE in athletes and controls respectively ($p=0.18$) (Figure 5). Furthermore, there was no difference between groups for the percentage of ventricular KE made up by vortex KE (early diastole $67\pm 1\%$ vs $71\pm 2\%$, $p=0.17$, diastasis $73\pm 2\%$ vs $70\pm 6\%$, $p=0.78$, late diastole $73\pm 2\%$ vs $71\pm 0.6\%$, $p=0.29$ for athletes and controls respectively).

Kinetic energy of the left and right side of the heart

There was a strong correlation between kinetic energy for the right and left side of the heart combining the atrial and ventricular KEs ($R^2=0.84$, $p<0.0001$), although KE was higher for the right side of the heart ($p<0.05$) (Figure 1B). The variations in kinetic energy over a cardiac cycle are shown in Figure 6A and B. When studying the sum of KE in the left atrium and left ventricle, there was no difference between athletes and controls for mean KE ($p=0.60$) or peak KE (systolic peak $p=0.19$, early diastolic peak $p=0.06$ and late diastolic peak $p=0.48$) (Figure 6A). Also for the right atrium and ventricle, there were no differences between groups for mean KE ($p=0.91$) or peak KE (systolic peak $p=0.29$, early diastolic peak $p=0.16$ and late diastolic peak $p=0.80$) (Figure 6B).

Rotational kinetic energy of the atria

Mean LA rotational KE did not differ between athletes and controls (athletes 0.60 ± 0.06 mJ, controls 0.47 ± 0.04 mJ, $p=0.19$). There was no difference between the fraction of rotational KE/total KE (athletes: $48\pm 2\%$, controls $46\pm 2\%$, $p=0.41$). During the early diastolic KE peak,

the average angle between net blood flow direction and the axis of rotation was 81° for athletes (range 64-112) and 91° for controls (range 61-128) ($p=0.19$), indicating mainly non-helical flow in both groups.

Mean RA rotational KE was similar between groups (athletes 0.83 ± 0.14 mJ, controls 0.81 ± 0.09 mJ, $p=0.72$). The rotational KE fraction of total KE did not differ between groups (athletes $47\pm 3\%$, controls $46\pm 2\%$, $p=0.88$). During the early diastolic KE peak, the average angle between flow direction and axis of rotation was 35° for athletes (range 8-90) and 37° for controls (range 9-63) ($p=0.33$).

Comparing LA rotational KE and RA rotational KE during early diastole, the angle between flow direction and rotation was significantly smaller in the RA ($p<0.0001$ for both groups), indicating more helical flow in the RA. This difference is illustrated in Figure 7, which shows a visualization of flow across the atrioventricular plane during peak early rapid filling.

Kinetic energy validation and effect of limited resolution

Validation of KE using PIV is shown in Figure 8A and B. A strong correlation and small bias were found ($y=0.89x+0.06$, $R^2=0.99$, $\text{mean}\pm 2\text{SD } -0.02\pm 0.12$ mJ). Figure 8C shows the change in measured KE when reducing the resolution by downsampling PIV data. Reducing the spatial and/or temporal resolution gives lower KE values. Figure 8D shows the change in measured KE in vivo in a healthy volunteer. Kinetic energy peaks appear lower for reduced spatial or temporal resolution.

DISCUSSION

This study shows that LV early diastolic KE is strongly associated with LVM, whereas for the right ventricle, RVEDV is the most important factor for RV early diastolic KE. These results indicate that the RV and LV have different filling mechanisms. Furthermore, athletes and controls have similar energy expenditure for pumping a given blood volume at rest which may be explained by a lower heart rate cancelling an increased KE per heart beat in athletes. In contrast to earlier findings using 2D-techniques, this study shows that the majority of LVKE is found within the vortex during diastole.

KE in the left side of the heart

Kinetic energy in early diastole was higher in athletes compared to controls and this was associated with larger LVM in athletes. The higher KE in early diastole in athletes may indicate enhanced diastolic function. A larger LVM can generate a more forceful suction causing blood to flow into the LV at higher velocities. The myocardium contains the elastic protein titin that acts like a “spring” which recoils back when the left ventricle relaxes. Thus, the physiologically increased myocardial mass in athletes with increased amounts of titin may recoil back faster, causing a more forceful aspiration of blood into the ventricle (2, 7, 24, 44).

In contrast to the physiological hypertrophy seen in athletes, pathologic hypertrophy such as hypertrophic cardiomyopathy is associated with an increased ventricular stiffness and impaired relaxation (16) due to adverse remodeling and fibrosis (5, 35). Thus, diastolic function is decreased (16) and therefore a decreased LVKE early diastolic peak can be expected in this group despite a large LVM. However, the pattern of kinetic energy over a cardiac cycle in patients with hypertrophic cardiomyopathy remains to be explored.

Systolic LVKE was lower than what was seen for the right ventricle. It has been shown that the difference is related to a longer outflow tract in the right ventricle compared to the left (11). Although there are high amounts of KE in the aorta, it is not considered a part of LVKE as it is seen distal to the aortic valve.

KE in the right side of the heart

Multiple linear regression analysis showed RVEDV as an independent predictor of the RV early diastolic peak. The RV is to a large extent filled by the movement of the AV-plane away from the apex, whereby it slides over a blood volume already in the atrium (2, 11, 33, 34). Thus, the blood volume has only a low velocity and therefore its mass, determined by RVEDV, has greater importance and is the main determinant of KE. A larger RVEDV, as seen in athletes, yields a larger blood volume and thus a higher KE.

Energy expenditure

At rest the metabolic demand of the average person, both athlete and control, is met by a cardiac index of approximately 3 l/min/m² in normal subjects as well as elite athletes (9). To estimate the amount of KE used to achieving enough cardiac output to meet the metabolic demands and compare between groups, we therefore divided the mean KE by cardiac index. There were no differences between athletes and controls, indicating that at rest the kinetic energy expenditure for intra-cardiac blood flow is similar between the healthy untrained heart and the large, healthy well trained heart. The lower heart rate may allow blood flow through the heart at a lower velocity which decreases KE despite a larger blood mass in athletes, thus cancelling out a higher KE per heartbeat. The similarities between controls and athletes further strengthen the concept that the athletes' heart is a physiological and healthy adaptation to long-term training.

Cardiac work during exercise

The external cardiac work performed by the heart is used to deliver a pressurized volume of blood into the circulation. It is divided into stroke work that constitutes approximately 99% of the LV work (28, 32) at rest, leaving <1% to kinetic energy, the work performed to accelerate blood. With increasing heart rate there is no diastasis between early diastolic filling and atrial contraction. As shown in the exercise model presented by Carlsson et al. (11), kinetic energy amounts to 3% of LV work and 24% of total RV work, indicating an increased importance of kinetic energy during exercise, in particular for the RV. We propose that during exercise, the improved diastolic suction seen in endurance athletes (43) allows for the blood to increase its kinetic energy more than is possible for untrained controls or for patients with diastolic heart failure. This could be one of the mechanisms by which the athlete's heart is able to deliver such large blood volumes at high heart rates. This, however, remains to be investigated.

Early diastolic vortex ring KE

Vortex rings grow by incorporating surrounding fluid, a phenomenon known as mixing (41). The energy inside the vortex ring is therefore a product of interactions between inflowing blood and remaining ventricular blood from end-systole. Vortex formation has been shown to redirect part of the inflowing blood towards the aortic valve which has been suggested to facilitate ventricular ejection (15) and allowing the ventricle to save energy as opposed to the energy it would cost to accelerate stationary blood. However, this concept has been challenged (29) and using a heart simulation model, Watanabe et al. (42) found that the vertical flow path did not have any energy-saving effect. Although the function of the diastolic vortex remains unclear, vortex formation may become a useful tool in early diagnosis of several cardiac diseases that affect ventricular geometry and function (18, 30). As

shown in a 4D PC-MR study by Föll et al. (18) significant differences in diastolic vortex formation can be seen between young and old subjects that indicate age-related early diastolic dysfunction. Furthermore, Agati et al. (1) used echo-PIV analysis and showed in a small study of patients with ST-elevation myocardial infarction that there is a difference in energy dissipation and vortex dynamics between healthy controls and patients as well as between patients with varying degree of LV dysfunction.

The similar results seen over the whole study population in the present study indicate that the physiological adaptations to long-term endurance training are balanced and the structures increase proportionally in size which allows for a maintained function and normal vortex formation. These results are in line with results presented by Gharib et al. (20) who demonstrated the robustness of optimal vortex formation and also suggested that pathologies would be reflected by changes in this parameter. In line with this hypothesis, vortex formation has been shown to differ in patients with acute myocardial infarction (1).

In this population with a large range of ventricular volumes, the energy inside the diastolic vortex was approximately 70% of the total diastolic energy with a range 60-80%. This differs from Bermejo et al. (6) who found vortex KE to be 26% of late-diastolic total KE with a range of 1-74% using echocardiography. One reason for the discrepancy can be that the methodologies differ. We used 4D-PC MR measuring three-directional velocities and three-dimensional volumes over time. Bermejo et al. used in-plane two-dimensional echocardiography measurements and derived the vortex KE and total KE using several assumptions including an elliptical mitral valve, circular LVOT and toroidal vortex ring shape. Bermejo et al. derived KE within the vortex core and the possibility of larger KE within the entire vortex was acknowledged by the authors. We measured KE within the entire

three-dimensional vortex and validated the results with in-vitro particle imaging velocimetry and found higher values with a narrow range in healthy subjects independent of ventricular size.

Helical vs. non-helical flow across the atrioventricular plane

We observed helical blood flow from the right atrium into the RV, but non-helical flow from the LA into the LV. A similar finding has previously been reported by Arvidsson et al. (2) in a cohort of healthy volunteers. Helical flow in the right heart is a consequence of the spatially offset configuration of the caval vein orifices in the RA, which produce a rotational flow pattern, first described using phase-contrast MRI by Kilner et al. (25). During ventricular filling, this rotational flow is redirected through the tricuspid valve, thereby changing into a helix. Rotational flow conserves energy to a larger degree compared to straight flow, which may assume greater significance during exercise (2). The similarity of helical flow in athletes and controls indicates that this mechanism is present in healthy hearts over a wide size range. The physiological importance of rotational/helical flow in the right heart remains to be investigated during exercise.

Validation of 4D PC kinetic energy calculations using PIV

The strong correlation and low bias for 4D PC measurements of KE as compared to PIV shows that present results are not influenced by a major bias or uncertainty. This also validates previous studies using the same methodology (2, 19). A recent validation study showed that 4D PC can underestimate peak velocities and therefore also KE peaks due to low temporal and spatial resolution (38), and a previous study suggested that accelerated readout techniques may also significantly underestimate peak velocities (12). The present KE validation results show that measurements at high KE tend to be slightly underestimated, and

that the effect is exacerbated by lowered temporal and spatial resolution. Therefore, the effects of temporal and spatial resolution must be considered when comparing KE values obtained using different 4D PC sequences. For longitudinal studies, it is likely of importance to settle for a consistent spatial resolution between subjects and examinations. Furthermore, resolution effects should especially be considered for measurements during exercise when KE can be expected to increase. To optimize data quality, achieving high spatial and temporal resolution should be points of focus when developing new 4D PC sequences for accurate KE quantification.

Limitations

Due to the retrospective inclusion of healthy normal subjects, there were subjects in the control group that were examined using different scanners and different field strengths compared to athletes. However, a previously performed validation of the two scanners showed similar results for KE and bias between scans were low (11). Furthermore, control subjects did not undergo exercise testing and their fitness status is based on personal communication.

Conclusions

Athletes have higher early left ventricular and right ventricular diastolic peak KE compared to untrained controls. Left ventricular mass is the main determinant of LV diastolic peak KE, as a larger LVM can create a larger restoring force that aspirates blood into the ventricle at high velocities. The RV fills mainly by basal displacement of the AV-plane. Thus, the blood volume has only a low velocity and therefore its mass, determined by RVEDV, has greater importance and is the main determinant of KE. There is no difference in mean KE indexed for CI, suggesting similar energy expenditure between athletes and controls for delivering a given

blood volume. This suggests that a lower heart rate in athletes cancels a higher KE per heartbeat. Left ventricular diastolic vortex KE did not differ between groups indicating that the physiological remodelling caused by long-term endurance training does not affect cardiac function with respect to vortex formation.

TABLES

Table 1. Subject characteristics and cardiac volumes. Mean \pm SD

	Men		Women	
	Controls n = 8	Athletes n = 6	Controls n = 6	Athletes n = 8
Age (years)	26 \pm 2	23 \pm 3	33 \pm 10	25 \pm 5
Weight (kg)	83 \pm 13	73 \pm 9	67 \pm 7	57 \pm 7 *
Height (cm)	185 \pm 9	183 \pm 8	167 \pm 6	166 \pm 7
BSA (m²)	2.07 \pm 0.20	1.92 \pm 0.16	1.75 \pm 0.11	1.62 \pm 0.12
HR (bpm)	63 \pm 7	51 \pm 10 *	60 \pm 9	51 \pm 3 *
THV (ml)	837 \pm 125	1120 \pm 179 **	681 \pm 51	761 \pm 83
LVM (g)	120 \pm 14	179 \pm 36 **	90 \pm 8	109 \pm 15 *
RVM (g)	27 \pm 4	38 \pm 5 **	21 \pm 5	29 \pm 3 **
LVEDV (ml)	198 \pm 38	250 \pm 32 *	157 \pm 16	175 \pm 26
RVEDV (ml)	223 \pm 31	290 \pm 42 *	165 \pm 23	199 \pm 33 *
LVSV (ml)	117 \pm 21	154 \pm 17 *	97 \pm 12	106 \pm 16
RVSV (ml)	115 \pm 19	148 \pm 11 *	93 \pm 10	114 \pm 24
CO (l/min)	7.3 \pm 1.6	7.9 \pm 2.1	5.8 \pm 1.2	5.4 \pm 1.0
CI (l/min/m²)	3.5 \pm 0.6	4.1 \pm 1.1	3.3 \pm 0.6	3.3 \pm 0.6
LVEF (%)	60 \pm 5	62 \pm 6	62 \pm 4	61 \pm 4
RVEF (%)	52 \pm 6	52 \pm 2	57 \pm 5	54 \pm 5
LA peak volume (ml)	92 \pm 20	128 \pm 34 *	83 \pm 15	92 \pm 13
RA peak volume(ml)	129 \pm 26	178 \pm 41 *	115 \pm 19	105 \pm 21
LVAVPD (mm)	16.3 \pm 0.3	15.9 \pm 1.7	14.9 \pm 1.4	14.9 \pm 1.9
RVAVPD (mm)	21.8 \pm 4.7	22.5 \pm 1.5	21.4 \pm 1.0	21.9 \pm 2.7

BSA – body surface area, g – gram, HR – heart rate, kg – kilogram, LA peak – left atrial peak volume, LVAVPD – left ventricular atrioventricular plane displacement, LVEDV – left ventricular end-diastolic volume, LVM – left ventricular mass, m – meter, min – minute, ml – milliliter, RA peak – right atrial peak volume, RVAVPD – right ventricular atrioventricular plane displacement, RVEDV – right ventricular end-diastolic volume, THV – total heart volume, VO₂peak – peak oxygen uptake

* p < 0.05 when compared to gender matched controls

** p < 0.01 when compared to gender matched controls

Table 2. Mean and peak kinetic energy in athletes and controls.

	Controls n=14	Athletes n=14
Mean kinetic energy (mJ)		
Left ventricle	1.8±0.2	2.1±0.3
Left atrium	1.0±0.1	1.3±0.1
Right ventricle	2.0±0.2	2.4±0.3
Right atrium	1.7±0.2	1.7±0.2
Left heart	2.9±0.2	3.3±0.4
Right heart	3.7±0.3	4.1±0.5
Peak systolic kinetic energy (mJ)		
Left ventricle	3.6±0.3	5.0±0.6
Left atrium	1.4±0.2	2.3±0.3**
Right ventricle	6.5±0.6	9.3±1.5
Right atrium	3.9±0.4	4.6±0.6
Left heart	4.6±0.3	6.0±0.7
Right heart	9.3±0.6	12.4±1.8
Peak early diastolic kinetic energy (E-wave) (mJ)		
Left ventricle	5.9±0.4	8.9±1.1*
Left atrium	3.5±0.3	4.5±0.6
Right ventricle	3.1±0.4	4.2±0.5*
Right atrium	2.8±0.3	3.2±0.4
Left heart	9.2±0.6	13.1±1.5
Right heart	5.6±0.5	7.2±0.8
Peak late diastolic kinetic energy (A-wave) (mJ)		
Left ventricle	1.1±0.1	1.1±0.1
Left atrium	0.8±0.1	0.8±0.1
Right ventricle	1.0±0.2	1.2±0.2
Right atrium	0.9±0.1	0.9±0.2
Left heart	1.8±0.3	1.9±0.2
Right heart	1.8±0.2	2.0±0.3

* p <0.05 when compared to controls

** p<0.01 when compared to controls

Table 3. Univariate and stepwise multiple linear regression analysis for LV and RV with peak early diastolic KE as dependent variable.

	Univariate regression R²	p-value	Multivariate regression β	p-value
Left ventricle				
LVM (g)	0.81	<0.0001	0.81	<0.0001
LVSV (ml)	0.75	<0.0001	0.29	0.13
LVEDV (ml)	0.76	<0.0001	0.26	0.24
LVSV _{long} (ml)	0.55	0.003	-0.06	0.71
Right ventricle				
RVEDV (ml)	0.87	<0.0001	0.87	<0.0001
RVSV _{long} ml)	0.87	<0.0001	0.42	<0.05
RVSV (ml)	0.80	<0.0001	0.03	0.89
RVM (g)	0.68	<0.0001	-0.19	0.32

Table 4. Stepwise multiple linear regression analysis for LA and RA with peak systolic KE as dependent variable.

	β	p
Left atria		
LVSV (ml)	0.626	<0.0001
LVSV _{long} (ml)	0.267	0.236
LV PER (m s ⁻¹)	-0.099	0.638
Right atria		
RVSV _{long} (ml)	0.748	<0.0001
RV PER (m s ⁻¹)	0.105	0.735
RVSV (ml)	-0.14	0.966

Figure legends

*Figure 1. Kinetic energy over a cardiac cycle in the four chambered heart. Panel A: Left ventricular KE where the early diastolic peak was higher in athletes. Panel B: Right ventricular KE where the early diastolic peak was higher in athletes. Panel C: Left atrial KE where the systolic peak was higher in athletes. Panel D: Right atrial KE where the peaks did not differ between athletes and controls. Error bars denote Mean \pm SEM. * $p < 0.05$ when compared to controls.*

Figure 2. Correlation between left and right ventricular KE (Panel A) and between the combined KE of the left ventricle and left atrium versus the right ventricle and right atrium (Panel B). Dashed line indicates line of identity. Mean left and right ventricular KE did not differ ($p=0.4$), however when comparing the left side of the heart with the right, right heart mean KE was higher ($p < 0.05$).

*Figure 3. Mean kinetic energy normalized for stroke volume in the ventricles (Panel A) and atria (Panel B). Right atrial KE normalized for RVSV was higher in controls compared to athletes. There was no difference between groups for LVKE normalized for LVSV ($p=0.51$), RVKE normalized for RVSV ($p=0.40$) or LAKE normalized for LVSV ($p=0.84$) * $p < 0.05$.*

Figure 4. Mean left ventricular KE indexed for cardiac index (Panel A) cardiac output (panel B) and stroke volume normalized for body surface area (Panel C). There was no difference between athletes and controls indicating similar energy expenditure between groups for pumping a given blood volume.

Figure 5. Kinetic energy inside the diastolic vortex divided by total ventricular diastolic energy in athletes and controls. There was no difference between groups, indicating that the morphological adaptations to long-term endurance training allows for preserved relations between ventricle and vortex.

Figure 6. Kinetic energy over a cardiac cycle in the left heart defined as the sum of kinetic energy in the LA and LV (Panel A) and in the right heart defined as the sum of kinetic energy in the RA and RV. When comparing total left and right heart KE between athletes and controls, no differences were seen. Data is presented as mean \pm SEM.

Figure 7. Streamline visualization of flow across the atrioventricular valve plane at peak early rapid filling of the ventricles. Left panel: 4 chamber view. Right panel: Short-axis view. The right side of the heart revealed helical flow across the tricuspid valve. Conversely, the left heart flow pattern is mainly linear across the mitral valve. The helicity of the flow did not differ between controls and athletes (see text for details). Streamline color indicates velocity.

Figure 8. Validation of KE using particle imaging velocimetry (PIV). A: Scatter plot of KE measured using 4D flow MR and PIV. B: Difference in KE measured using MR and PIV plotted against PIV KE. A strong correlation and small bias were found. C: Change in KE for reduced resolution in PIV phantom data. Each curve shows reduction in KE for different voxel sizes. Reducing spatial and/or temporal resolution result in lower measured KE values. D: Change in KE curves in a healthy volunteer for reduced resolution. Reduced spatial and/or temporal resolution gives lower peak KE values. The resolution analysis in Panels C and D was performed by downsampling already acquired data.

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