ECHOCARDIOGRAPHIC CHARACTERIZATION OF THE INFERIOR VENA CAVA IN TRAINED AND UNTRAINED FEMALES

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FULL TITLE

Echocardiographic characterization of the inferior vena cava in trained and untrained females

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ABSTRACT

We aimed to explore inferior vena cava (IVC) long- and short-axis dimensions, IVC shape and collapsibility in 46 trained and 48 untrained females (mean age 21±2 years).

Echocardiography in the subcostal view revealed a larger expiratory long-axis diameter (mean 24±3 vs. 20±3 mm, p<0.001) and short-axis area (mean 5.5±1.5 vs. 4.7±1.4 cm², p=0.022) in trained females. IVC shape (the ratio of short-axis major-to-minor diameter) and the relative decrease in IVC dimension with inspiration was similar between groups. The IVC long-axis diameter reflected short-axis minor diameter and was correlated to maximal oxygen uptake (r=0.52, p<0.01). In summary, our results indicate that trained females exhibit a larger IVC with similar shape and respiratory decrease in dimensions as untrained females. The long-axis diameter corresponded closely to short-axis minor diameter and thus underestimates maximal IVC diameter.

KEYWORDS

Inferior Vena Cava, Echocardiography, Athlete’s heart, Exercise Training, Sports Cardiology, Maximal Oxygen Uptake
INTRODUCTION

The effect of chronic endurance exercise upon cardiac dimensions is well acknowledged, and abundant echocardiographic studies have provided evidence for a physiologic increase in atrial and ventricular dimensions in both male and female endurance athletes compared to sedentary subjects (Pelliccia et al. 1996, Pluim et al. 2000, D'Andrea et al. 2013, D'Ascenzi et al. 2014, Hedman et al. 2015). Furthermore, recent comprehensive reviews describe evidence for larger dimensions of peripheral arteries (Green et al. 2012) and of the aortic root (Iskandar and Thompson 2013) in endurance athletes. Only a few studies provide evidence in support of a larger inferior vena cava (IVC) in trained than in untrained subjects (Zeppilli et al. 1995, Goldhammer et al. 1999, Erol and Karakelleoglu 2002, D'Ascenzi et al. 2013), although these findings remain to be verified in female athletes.

The diameter of the IVC is, together with the extent of IVC collapse during inspiration, used for estimation of right atrial (RA) pressure (Lang et al. 2015). The finding of a dilated IVC in an endurance athlete is suggested to represent a physiologic adaptation to repeated, intermittent volume loading and not to reflect an increased RA pressure (D'Ascenzi et al. 2013). In theory, it is possible that the highly compliant, dilated IVC is somewhat collapsed in athletes during resting conditions when cardiac output is similar in trained and untrained subjects. This could affect echocardiographic measures of IVC diameter obtained in a single plane. Previous measurements of IVC diameter and collapsibility in athlete-control comparisons are limited to measurements in the subcostal long-axis view (LAX) and thus, possible differences in IVC shape are not accounted for. Extending the IVC examination to the cross-sectional short-axis view (SAX) could provide additional information on two-dimensional IVC dimensions, including IVC area and shape.
Our main purpose was to characterize and compare the IVC size, shape and respiratory decrease in dimensions in both the long- and short-axis views in trained and untrained females. Our secondary aims were to compare corresponding long- and short-axis IVC measurements and to relate IVC dimensions to maximal oxygen uptake (VO$_{2\text{max}}$).

**METHODS**

**Subjects**

We included 94 healthy, non-pregnant, non-smoking females younger than 26 years. All subjects were screened for cardiovascular disease, including a resting ECG, and underwent maximal bicycle ergometer testing. Forty-six females were endurance trained (ATH), currently trained 13±5 (mean±SD) hours per week and had been competing for 6±2 years at a national or regional level in a variety of endurance sports (17 orienteers, 6 middle and long-distance runners, 5 triathletes, 5 canoeists, 4 biathletes, 3 cyclists, 3 swimmers, 3 handball players). The remaining 48 females were high school and college students not engaged in regular endurance or resistance training for several years prior to the study (CON). Of these, 18 were categorized as ‘normally active’, including e.g. subjects riding a bike or walking to school, while 33 negated any regular physical activity and were categorized as ‘inactive’.

In all subjects, the use of oral or implantable contraceptives was recorded, as well as number of days since the first day of latest menstruation. The phase of menstruation cycle was then categorized as either of the following: (a) no regular menstruation; (b) early follicular phase (day 1-7); (c) late follicular phase (day 8-14); (d) early luteal phase (day 15-21); (e) late luteal phase (day ≥22). The menstruation cycle phases were further dichotomized into follicular phase (categories a+b above) and luteal phase (c+d).
Informed consent was obtained from all subjects. The study was approved by the regional ethical review board in Linköping, Sweden.

**Echocardiography**

Standard echocardiographic investigation was performed with subjects resting in the lateral decubitus position using commercially available standard equipment with offline storage (Vivid 7/Vivid E9 and EchoPAC version BT 11, GE Healthcare, Horten, Norway). Athletes were instructed to refrain from strenuous exercise at least 24 hours prior to the examination. Standard two-dimensional (2D) and M-mode echocardiography were applied in accordance with current recommendations (Lang et al. 2015), and our protocol for cardiac measurements has been described in detail previously (Hedman et al. 2015, Hedman et al. 2015). In brief, we determined ventricular dimensions in diastole, and atrial areas in systole using 2D echocardiography. The modified Simpson biplane technique was used for calculating left ventricular end-diastolic volume (LVEDV)(Lang et al. 2015).

**Inferior vena cava**

Subjects were examined in the supine position, lying on a horizontally levelled examination table with a small pillow as head support, and images were obtained in the standard subcostal view. Images from three consecutive respiratory cycles were recorded during quiet respiration, without a sniff maneuver. Measurements of IVC dimensions were performed off-line by the same investigator, and all measurements were determined as maximal dimension during expiration (EXP) and minimal dimension during inspiration (INSP) within the one respiratory cycle with the most optimal image quality (Figure 1).

In the long-axis view, IVC diameters were determined perpendicular to the IVC long-axis (LAX\textsubscript{EXP} and LAX\textsubscript{INSP}), proximal to the junction with the hepatic vein approximately three
centimeters from the RA (Figure 2). Short-axis dimensions were determined in images obtained after a 90° rotation of the transducer, aiming at recording long- and short-axis measurements at the same position. Special care was taken to obtain a short-axis plane perpendicular to the long-axis, i.e., where the area was smallest and not falsely too large because of angulation. Maximal IVC area during expiration (SAXEXP-AREA) was determined first, followed by major-axis IVC diameter, defined as the largest IVC diameter at maximal area (SAXEXP-MAJOR). Minor-axis diameter was defined as the largest IVC diameter perpendicular to the major-axis diameter (SAXEXP-MINOR). Finally, the same measurements were applied at minimal area during inspiration (SAXINS-AREA, SAXINS-MAJOR and SAXINS-MINOR, respectively).

The IVC shape during expiration and inspiration was calculated as the ratio between SAX major-to-minor diameter (SAXEXP-MAJOR / SAXEXP-MINOR and SAXINS-MAJOR / SAXINS-MINOR respectively). The inspiratory decrease in IVC dimension (%) for each measure was calculated as (100 × [expiratory dimension - inspiratory dimension] / expiratory dimension) and for long-axis diameter, this has previously been termed the IVC collapsibility index (Lang et al. 2015).

In order to reduce the influence of differences in body size between the groups, IVC area was indexed by body surface area (BSA) and IVC diameter by square-rooted BSA, adopting the suggested approach of indexing in the same dimension as measured (Batterham and George 1998).

**Statistical analysis**

Normally distributed continuous data were expressed as mean±SD (5th – 95th percentiles) and non-normally distributed continuous data were expressed as median (25th – 75th percentiles). Between-group differences were tested with Student’s t-test or Mann-Whitney U test, while
within-group differences were tested with paired t-test or Wilcoxon signed rank test. Frequencies were cross-tabulated and differences between groups were tested with the Chi² test. Bivariate correlation analysis was performed to explore how VO₂max, LVEDV and RA area correlated to IVC dimensions and to IVC shape and collapsibility. Differences were tested two-sidedly, and a p-value ≤0.05 was considered statistically significant. Results were analyzed using SPSS Statistics 22 (IBM Software, USA).

Inter- and intraobserver variability was tested in 16 randomly selected subjects for SAXEXP-AREA and four linear measures of IVC diameter. The coefficient of variation (% COV) was calculated as follows: (√(Σdᵢ²/2n)) / (overall means), where dᵢ is the difference between the i:th paired measurement and n is the number of differences (Dahlberg 1948). In addition, the single measure intraclass correlation coefficient (ICC) was calculated for inter and intraobserver variability in an absolute agreement two-way mixed model.

RESULTS

Data quality and reproducibility

Image quality permitted long-axis measures in 87 subjects (44 ATH) and short-axis measurements were possible in 80 subjects (41 ATH). In total, 87 % of 752 possible measurements could be obtained. Mean intraobserver variability (with ICC) for long-axis IVC diameter was 7.1 % (0.91), short-axis diameter 5.4 % (0.92) and for SAXEXP-AREA 6.5 % (0.95). Mean interobserver variability (ICC) for long-axis IVC diameter was 9.9 % (0.81), short-axis diameter 10.5 % (0.69) and for SAXEXP-AREA 13.7 % (0.80).

Subject characteristics and standard echocardiographic measures

Mean age was similar between groups (both 21±2 years, p=0.743), while ATH were taller (1.68±0.06 vs 1.66±0.05 m, p=0.028) and had larger body surface area than CON (1.69±0.10
vs 1.63±0.09 m², p=0.008). The cardiorespiratory conditioning of ATH was reflected in a lower heart rate at rest (54±8 vs 71±10 beats × min⁻¹, p<0.001) and higher VO₂max (52±5 vs 39±5 mL × kg⁻¹ × min⁻¹, p<0.001) than in CON. In total, 41 (44%) subjects used contraceptives, and there was no difference in contraceptive usage between ATH and CON (n=20 vs. n=21, p=0.979). Data on menstruation cycle were available in all but one subject (ATH). Seven ATH (16%) and five CON (10%) reported no or irregular menstruation. The proportion of subjects in each of the five categories outlined in ‘Methods’ did not differ between trained and untrained subjects (Chi², p=0.877) nor did the proportion of subjects in dichotomized follicular and luteal categories (Chi², p=0.463).

All left and right ventricular and atrial dimensions were larger in ATH, with and without indexing by BSA, as has been described in detail previously (Hedman et al. 2015). Absolute RA area was 39 % larger in ATH (15.7±2.7 vs 11.3±1.9 cm², p<0.001) and LV end-diastolic volume was 32 % greater in ATH (114±19 vs 86±13 mL, p<0.001) than in CON. No subject in either group presented with any significant valvular pathology.

**Inferior vena cava measurements**

*Athletes versus controls*

Athletes had significantly larger LAX diameter and SAX area than CON, upon both expiration and inspiration (table 1). LAX_EXP and LAX_INSPIR were 17 % and 15 % larger in ATH than in CON, respectively, while SAX_EXP-AREA and SAX_INSPIR-AREA were 17 % and 27 % larger in ATH than in CON. Following indexing by the proper dimension of BSA, LAX_EXP was 14 % larger and SAX_INSPIR-AREA 24 % larger in ATH than in CON, respectively.

*Long-axis versus short-axis measurements*
Long-axis IVC diameter corresponded more closely to SAX minor dimension than to SAX major dimension both upon inspiration and expiration (Figure 3). Bland-Altman plots are presented in Supplementary Figure 1. Both SAXEXP-MAJOR and SAXINSPI-MAJOR were larger than the corresponding LAX diameter (both p<0.001), while SAXEXP-MINOR and SAXINSPI-MINOR were similar to the corresponding LAX diameter (both p>0.1).

Inferior vena cava shape and inspiratory dimensional decrease

There was no statistically significant between-group difference in the inspiratory decrease in any IVC dimension. The IVC collapsibility index (i.e. relative decrease in subcostal long-axis diameter) was 29±15 vs 28±17 % in ATH and CON, respectively (p=0.785), while SAX major dimension decreased 21±13 % in ATH versus 25±13 % in CON (p=0.169) and SAX minor dimension decreased 23±14 % in ATH versus 29±17 % in CON (p=0.106). Short-axis area decreased 40±17 % in ATH versus 45±18 % in CON (p=0.185).

There was no difference between groups in the ratio of SAX major-to-minor dimension (Figure 4). In the whole sample of subjects, IVC shape was similar at SAXEXP-AREA, 1.3 (1.2-1.5), and SAXINSPI-AREA, 1.4 (1.2-1.6), p=0.054. At SAXEXP-AREA, only one control subject had a ratio >2.0 (2.1), while three controls and one athlete had a ratio >2.0 at SAXINSPI-AREA (2.1-2.6).

Inferior vena cava correlations

In the whole sample of females, LAXEXP was the IVC dimension that correlated most strongly to VO2max (Figure 5), LVEDV and RA area. The correlations were moderate (VO2max r=0.52, LVEDV r=0.46, RA area r=0.49, all p<0.001). There was no correlation between VO2max, LVEDV or RA area to IVC shape or to the relative decrease in IVC dimension.
The relative decrease in IVC long-axis diameter with inspiration correlated negatively with \( \text{LAX}_{\text{EXP}} \) \((r=-0.311, p<0.03)\) and the relative decrease in SAX area correlated negatively with \( \text{SAX}_{\text{EXP AREA}} \) \((r=-0.275, p<0.014)\).

**DISCUSSION**

**IVC dimensions in trained versus untrained subjects**

The most common measure of IVC dimension, recommended by current guidelines, is \( \text{LAX}_{\text{EXP}} \), measured in the subcostal echocardiographic view (Lang et al. 2015). To our knowledge, this measure has not previously been compared in trained versus untrained females and we found that this measure was 17 % larger in ATH than in CON, and it remained 15 % larger in ATH after indexing by square-rooted BSA. In addition, by extending IVC measures to the short-axis view, we could, for the first time, report a larger IVC cross-sectional area in endurance athletes.

Our results confirm findings from studies on predominately male subjects (Zeppilli et al. 1995, Goldhammer et al. 1999, Erol and Karakelleoglu 2002, D'Ascenzi et al. 2013). The only study that explicitly presents maximal subcostal IVC long-axis diameter in trained subjects found male cyclists, long-distance runners and volleyball players to have a mean IVC diameter of 28, 28 and 27 mm, respectively (Zeppilli et al. 1995). Dividing these measures by square-rooted BSA of the subjects yields indexed values of 20, 20 and 18 mm \( \times \) m\(^{-1}\), respectively, with the corresponding value in our sample of female athletes being 18±2 mm \( \times \) m\(^{-1}\). Thus, although males have larger absolute IVC diameter, this difference would seem to be almost eradicated when accounting for body size.

In a recent study by D’Aszenci et al. (2014), IVC long-axis diameter in 24 professional female volleyball players increased from 17 to 21 mm (22 %) after 16 weeks of intensive
training following a period of detraining. This was a larger relative increase than in left and right atrial area. In our sample of females, we have previously reported linear left and right ventricular cavity dimensions to be 7-11 % and 10-15 %, respectively, larger in ATH than in CON (Hedman et al. 2015). When viewed together, current evidence indicates a substantial increase in IVC long-axis diameter following endurance training.

**Influence of training on IVC dimensions - possible mechanisms**

Blood flow in the IVC during submaximal supine cycling has been found to increase three-fold at a workload where cardiac output doubled from resting values (Nielsen and Fabricius 1968), which implies that the IVC is exposed to larger variations in hemodynamic load than the left and right heart chambers. The intermittent increases in arterial wall shear stress and cardiac biomechanical stress seen with repeated bouts of endurance exercise have been found to induce arterial and cardiac chamber dilation, respectively, through local endothelial factors (Green et al. 2012) and myocyte elongation due to neuro-humoral signaling (Hill and Olson 2008). As the walls of large veins are much thinner and structurally different from the walls of large arteries (Basu et al. 2010, Isayama et al. 2013), and are differently innervated (Amenta et al. 1982), it is plausible that the mechanisms behind IVC dilation are distinct from other cardiovascular adaptations to endurance exercise. However, the mechanisms underlying chronic IVC dilation in endurance trained subjects have not been established.

Assuming RA pressure is similar in trained and untrained subjects (as discussed in next subsection), other physiological adaptations seen with exercise training must account for the influence on IVC dimensions at rest.

First, IVC dimension is influenced by hydration status, diminishing with dehydration (Dipti et al. 2012, Zhang et al. 2014). Recently, Waterbrook et al. (2015) reported a ~14 % mean decrease in IVC maximal long-axis diameter accompanied by a 1.5 % mean weight loss in 26
male American football players following a three hour training session (Waterbrook et al. 2015). It is possible that the commonly reported 10 % larger blood volume in endurance athletes (Convertino et al. 1991, Sawka et al. 2000) could increase IVC dimension at rest, especially in the supine position when part of the venous blood pool is redistributed from the legs to the thorax. Interestingly, Miyachi et al. (2001) demonstrated that 240 minutes one-legged cycling per week during a six week period increased cross-sectional area of the femoral vein, not only in the exercised leg, but also to a lesser extent in the control leg (Miyachi et al. 2001). This indicates a systemic adaptation to one-legged cycling, which could possibly be mediated through an increase in blood volume.

Second, endurance trained athletes present with an increased parasympathetic tone at rest (Shin et al. 1997), which theoretically could induce IVC dilation through direct parasympathetic innervation (Amenta et al. 1982). Interestingly, Styczynski et al. (2009) reported increased IVC diameter (25±2 vs 21±3 mm) in 53 young, predominately female non-athletes with a history of vasovagal syncope when compared to healthy age-matched subjects. This could imply a decrease in venous tone related to alterations in the autonomous nervous system, which has been described in patients with vasovagal syncope (Grubb 2005).

In summary, we believe that the increased blood volume commonly reported in endurance athletes could provide a plausible explanation to increases in IVC dimensions at rest in the supine position in this group, although slight differences in autonomous tone or RA pressure cannot be ruled out based on the current literature.

**IVC shape and respiratory decrease in dimensions**

We found that both ATH and CON had an equally shaped, slightly oval IVC at both expiration and inspiration and that the ratio of major-to-minor diameter at maximal area only exceeded 2.0 in one subject. These findings could be of interest since the role of IVC shape in
the diagnosis of and prognosis for trauma patients (Matsumoto et al. 2010, Johnson et al. 2013), as well as hemodialysis patients (Naruse et al. 2007) is emerging. Normal IVC shape in healthy subjects has, however, to our knowledge not yet been determined.

The relative decrease in IVC dimension, imposed by the negative intra-thoracic pressure following inspiration, is together with IVC diameter suggested as a non-invasive surrogate measure of RA pressure (Lang et al. 2015). We found a similar relative decrease in IVC dimensions during quiet inspiration in trained and untrained females. Thus, the dilated IVC in ATH was not associated with decreased IVC collapse compared to CON, which indicates similar RA pressures between groups, which is supported by our finding of similar IVC shape between groups, as IVC shape is related to IVC transmural pressure (Moreno et al. 1970). We and others (Goldhammer et al. 1999) report weak negative correlations between maximal IVC dimension and the respiratory decrease in dimension in ATH, which probably reflects a mathematical ratio issue, rather than an increased RA pressure, as previously discussed for flow-mediated dilation of arteries (Atkinson and Batterham 2013). There are previous reports of increased prevalence of regurgitation over the tricuspid valve in endurance athletes compared to controls (Douglas et al. 1989), which theoretically could alter RA pressure. However, no subject in either group had any significant valvular lesion.

An unchanged RA pressure in endurance athletes may be supported by cross-sectional studies reporting similar tricuspid E/e'-ratio in trained and untrained subjects (D'Ascenzi et al. 2013, Pagourelias et al. 2013) Similar RA pressures at rest have been reported in one small study utilizing right atrial catheterization in eight young subjects with varying VO₂max (Stickland et al. 2006), as well as in a recent study including 102 elderly subjects with differences in life-long exercise dose and current VO₂max (Bhella et al. 2014). In summary, we conclude that our findings together with previous research do not support an increase in resting RA pressure in trained individuals.
Long- versus short-axis measurements

An interesting finding was that LAX diameter corresponded more closely to SAX minor- than to major-axis diameter and that LAX measurements underestimated maximal IVC diameter during both expiration and inspiration (Figure 3 and Supplementary Figure 1). This could be an effect of a failure to align the echocardiographic beam to the widest part of the IVC in the longitudinal plane, an effect of the IVC being slightly oval or a combination of the two. The latter is supported by the observation that in addition to a slightly oval IVC, we also found the major-axis to be somewhat obliquely aligned relative to the transducer beam in most subjects (as seen in Figure 1). Our finding is in contrast to that of Moreno et al. (1984), who found no difference between maximal LAX and SAX diameter in a mixed sample of cardiac patients and healthy subjects. However, as no data on IVC shape was presented and a substantial part of the subjects had right heart disease and elevated RA pressure, this could have influenced the results. Our results suggest that in settings where the maximal IVC diameter is sought, short-axis measurements may be preferable to the standard long-axis diameter. In general, the short axis view of the IVC also circumvents the problem of alignment that one has to be aware of when using the long axis view.

Relation to VO2max, LVEDV and RA area

The IVC measurement correlating most strongly to VO2max, LVEDV and RA area was LAXEXP. We have previously reported stronger correlations between VO2max and LVEDV and RA area (r=0.71 and r=0.64, respectively) than found between VO2max and any measure of IVC size in the current study (Hedman et al. 2015b). This could imply that IVC dilation is secondary to systemic adaptations also affecting cardiac dimensions (and VO2max), while cardiac dimensions have a more direct effect upon VO2max. This may be further supported by
the observation that IVC dimension correlated similarly strongly to LVEDV and RA area as to VO\textsubscript{2max}, a finding reported previously by others (Goldhammer et al. 1999).

**Menstrual cycle and oral contraceptives**

Although there is a lack of extensive evidence that hemoglobin levels or plasma volume actually changes during the different phases of the menstrual cycle in female athletes (Janse de Jonge 2003), there are studies suggesting that such fluctuations occur in untrained females (Vellar 1974). In addition, the use of contraceptive has been associated with increased plasma volume in healthy females (Lehtovirta et al. 1977). There are no available studies investigating the influence of menstrual cycle phase or the use of contraceptives on IVC dimension, and this was beyond the scope of the current study. However, as there was no difference in the proportion of trained and untrained females using contraceptives, or in the distribution of subjects in different phases of the menstrual cycle, it is unlikely that this had any influence on the observed difference between groups in IVC dimensions reported in the current study.

**Limitations**

First, we chose to measure long-axis IVC diameter three centimeters caudal to the junction with the RA, in order to measure LAX diameter at the same position as SAX diameters. This may impose a limitation in comparing our long-axis diameters to those from previous athlete-control studies, which applied a more cranial approach, often one to two centimeters from the RA junction. However, the comparison between ATH and CON was not affected by this approach. Second, we did not use a sniff maneuver when determining the relative inspiratory decrease in IVC dimensions. However, measurements during quiet respiration have been found to discriminate a normal from an elevated RA pressure with similar accuracy (Brennan et al. 2007, Taniguchi et al. 2015). Third, although a majority of athletes were competitive at
the national level, not all could be termed top-level athletes as in previous studies (Zeppilli et al. 1995, Goldhammer et al. 1999). This would, however, rather underestimate than overestimate the difference between the trained and untrained subjects, supporting the notion that the IVC is indeed dilated in endurance trained females.

CONCLUSIONS

We found that IVC dimensions in both long- and short-axis views were larger in endurance trained than in untrained females, while the IVC was similarly shaped and showed a similar relative decrease in dimensions with inspiration in both groups. The IVC dimensions correlated positively with VO₂max and cardiac dimensions, suggesting increasing IVC dilation with increasing fitness, although the mechanisms underlying IVC dilation in trained subjects remains to be elucidated. Finally, we showed that IVC diameter measured in the long-axis view underestimated the maximal IVC diameter, and corresponded more closely to short-axis minor diameter.

ACKNOWLEDGEMENTS

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FIGURE CAPTIONS LIST

CAPTION, Figure 1

Image showing echocardiographic view of long-axis (panel A and panel B) and short-axis (panel C and panel D) maximal expiratory (panel A and C) and minimal inspiratory (panel B and panel D) inferior vena cava dimensions in one athlete.

CAPTION, Figure 2

Schematic illustration of inferior vena cava measurements during expiration (left) and inspiration (right). Short-axis measurements obtained following a 90° rotation of the transducer approximate to the level of diameter measurement in the long-axis view. Calculation of inferior vena cava shape outlined in box. IVC, inferior vena cava; LAX, long-axis; SAX, short-axis; EXP, expiration; INSP, inspiration.

CAPTION, Figure 3

Panel A shows the relation between maximal diameters obtained during expiration in long-axis view (y-axis) plotted against major- and minor-axis diameter from short-axis view (x-axis). Panel B shows the corresponding minimal measures during inspiration. Circles represent trained females, squares represent untrained females. Long-axis diameter corresponded more closely to short-axis minor than major diameter at expiration as well as at inspiration. LAX, long-axis; EXP, expiration; SAX, short-axis; INSP, inspiration.

CAPTION, Figure 4

Histogram showing the distribution of major-to-minor axis diameter ratio (i.e. shape) at maximal area during expiration (upper panel) and at minimal area during inspiration (lower panel). Red color denotes athletes and grey color control subjects, with median values for the
groups presented in the same color. A schematic illustration of corresponding ratio of a
cylinder with constant width is provided on x-axis. There was no between-group difference in
the median value of inferior vena cava shape during either expiration or inspiration.

**CAPTION, Figure 5**

Scatter-dot diagram with a linear regression line showing the relation between maximal
inferior vena cava diameter measured in the long-axis during expiration (LAX_{EXP}) and
maximal oxygen uptake (VO_{2max}). Red and grey color denote athlete and control subjects,
respectively.
### Table 1. Absolute and indexed inferior vena cava measurements during expiration and inspiration.

<table>
<thead>
<tr>
<th></th>
<th>Maximal dimension (expiration, mm)</th>
<th>Minimal dimension (inspiration, mm)</th>
<th>p-value</th>
<th>Maximal dimension (expiration, mm)</th>
<th>Minimal dimension (inspiration, mm)</th>
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<td><strong>Absolute measures</strong></td>
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<tr>
<td>LAX diameter (mm)</td>
<td>24±3 (19-31)</td>
<td>20±3 (15-26)</td>
<td>&lt;0.001</td>
<td>17±5 (10-28)</td>
<td>15±5 (7-23)</td>
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<td>SAX major diameter (mm)</td>
<td>31±5 (23-42)</td>
<td>29±5 (21-38)</td>
<td>0.054</td>
<td>24±5 (17-35)</td>
<td>22±5 (12-30)</td>
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<td>SAX minor diameter (mm)</td>
<td>23±4 (16-32)</td>
<td>22±4 (13-28)</td>
<td>0.155</td>
<td>18±5 (10-25)</td>
<td>16±5 (6-25)</td>
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<td>SAX area (cm²)</td>
<td>5.5±1.5 (3.1-8.2)</td>
<td>4.7±1.4 (2.4-7.4)</td>
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<td>2.7±1.2 (0.5-5.0)</td>
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<td><strong>Measures indexed by body surface area</strong></td>
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<td></td>
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</tr>
<tr>
<td>LAX diameter</td>
<td>18±2 (15-23)</td>
<td>16±3 (12-20)</td>
<td>&lt;0.001</td>
<td>13±4 (8-22)</td>
<td>12±4 (6-18)</td>
<td>0.065</td>
</tr>
<tr>
<td>SAX major diameter</td>
<td>24±4 (18-32)</td>
<td>22±4 (16-29)</td>
<td>0.131</td>
<td>19±4 (13-27)</td>
<td>17±4 (9-23)</td>
<td>0.044</td>
</tr>
<tr>
<td>SAX minor diameter</td>
<td>18±3 (12-25)</td>
<td>17±3 (10-22)</td>
<td>0.280</td>
<td>14±4 (8-19)</td>
<td>12±4 (5-19)</td>
<td>0.092</td>
</tr>
<tr>
<td>SAX area</td>
<td>3.4±1.4 (1.8-4.8)</td>
<td>2.7±1.2 (1.5-4.8)</td>
<td>0.020</td>
<td>2.0±0.9 (0.8-3.5)</td>
<td>1.6±0.8 (0.3-3.0)</td>
<td>0.042</td>
</tr>
</tbody>
</table>
Data presented as mean±SD (5th – 95th percentiles). *, indexing by the proper dimension of body surface area, as described in ‘Methods’. LAX, long-axis; SAX, short-axis.