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Original Contribution

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

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Abstract—The aim of the study was to explore the long- and short-axis dimensions, shape and collapsibility of the inferior vena cava in 46 trained and 48 untrained females (mean age: 21 ± 2 y). 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 cm^2, $p = 0.014$) in trained females. IVC shape (the ratio of short-axis major to minor diameters) and the relative decrease in IVC dimension with inspiration were similar for the two 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, the results indicate that trained females have a larger IVC similar in shape and respiratory decrease in dimensions to that of untrained females. The long-axis diameter corresponded closely to short-axis minor diameter and, thus, underestimates maximal IVC diameter. (E-mail: kristofer.hedman@liu.se) © 2016 The Authors. Published by Elsevier Inc. on behalf of World Federation for Ultrasound in Medicine & Biology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Key Words: **Inferior vena cava, Echocardiography, Athlete's heart, Exercise training, Sports cardiology, Maximal oxygen uptake.**

INTRODUCTION

The effect of chronic endurance exercise on cardiac dimensions is well acknowledged, and abundant echocardiographic studies have provided evidence of a physiologic increase in atrial and ventricular dimensions in both male and female endurance athletes compared with sedentary persons (D'Andrea et al. 2013; D'Ascenzi et al. 2014; Hedman et al. 2015b; Pelliccia et al. 1996; Pluim et al. 2000). 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 persons (D'Ascenzi et al. 2013; Erol and Karakelleoglu 2002; Goldhammer et al. 1999; Zeppilli et al. 1995), 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 persons. 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 (LAX) view, and thus, possible differences in IVC shape are not accounted for. Extending the IVC examination to the cross-sectional short-axis (SAX)

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view could provide additional information on 2-D IVC dimensions, including IVC area and shape.

Our main purpose was to characterize and compare the size, shape and respiratory decrease in dimensions of the IVC 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 ($VO_{2\ max}$).

METHODS

Subjects

We included 94 healthy, non-pregnant, non-smoking females younger than 26 y. All subjects were screened for cardiovascular disease, including a resting electrocardiogram, and underwent maximal bicycle ergometer testing. Forty-six females were endurance trained (ATH), currently training 13 ± 5 h/wk (mean ± standard deviation), and had been competing for 6 ± 2 y at a national or regional level in a variety of endurance sports (17 orienteers, 6 middle- and long-distance runners, 5 tri-athletes, 5 canoeists, 4 bi-athletes, 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 before the study (CON). Of these, 18 were categorized as "normally active," including, for example, females riding a bike or walking to school, whereas 33 negated any regular physical activity and were categorized as "inactive."

In all subjects, the use of oral or implantable contraceptives was recorded, as was the number of days since the first day of latest menstruation. The phase of the menstruation cycle was then categorized as either of the following: (i) no regular menstruation; (ii) early follicular phase (days 1–7); (iii) late follicular phase (days 8–14); (iv) early luteal phase (days 15–21); (v) late luteal phase (day ≥22). The menstruation cycle phases were further dichotomized into follicular phase (categories i + ii) and luteal phase (iii + iv).

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 h before the examination. Standard 2-D and M-mode echocardiography were performed in accordance with current recommendations (Lang et al. 2015). Our protocol for cardiac measurements has been described in detail previously (Hedman et al. 2015a, 2015b). In brief, we determined ventricular dimensions in diastole and atrial areas in systole using 2-D 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 leveled 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 offline 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 (Fig. 1).

In the long-axis view, IVC diameters were determined perpendicular to the IVC long axis (LAX_{EXP} and LAX_{INSP}), proximal to the junction with the hepatic vein approximately 3 cm from the right atrium (Fig. 2). Short-axis dimensions were determined in images obtained after a 90° rotation of the transducer, with the aim of recording LAX and SAX measurements at the same position. Special care was taken to obtain a SAX plane perpendicular to the long-axis, that is, where the area was smallest and not falsely too large because of angulation. Maximal IVC area during expiration ($SAX_{EXP\text{-}AREA}$) was determined first, followed by major-axis IVC diameter, defined as the largest IVC diameter at maximal area ($SAX_{EXP\text{-}MAJOR}$). Minor-axis diameter was defined as the largest IVC diameter perpendicular to the major-axis diameter ($SAX_{EXP\text{-}MINOR}$). Finally, the same measurements were applied at minimal area during inspiration ($SAX_{INSP\text{-}AREA}$, $SAX_{INSP\text{-}MAJOR}$ and $SAX_{INSP\text{-}MINOR}$, respectively).

The IVC shape during expiration and inspiration was calculated as the ratio of SAX major diameter to minor diameter ($SAX_{EXP\text{-}MAJOR}/SAX_{EXP\text{-}MINOR}$ and $SAX_{INSP\text{-}MAJOR}/SAX_{INSP\text{-}MINOR}$, 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).

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 means ± standard deviations (5th–95th percentiles),

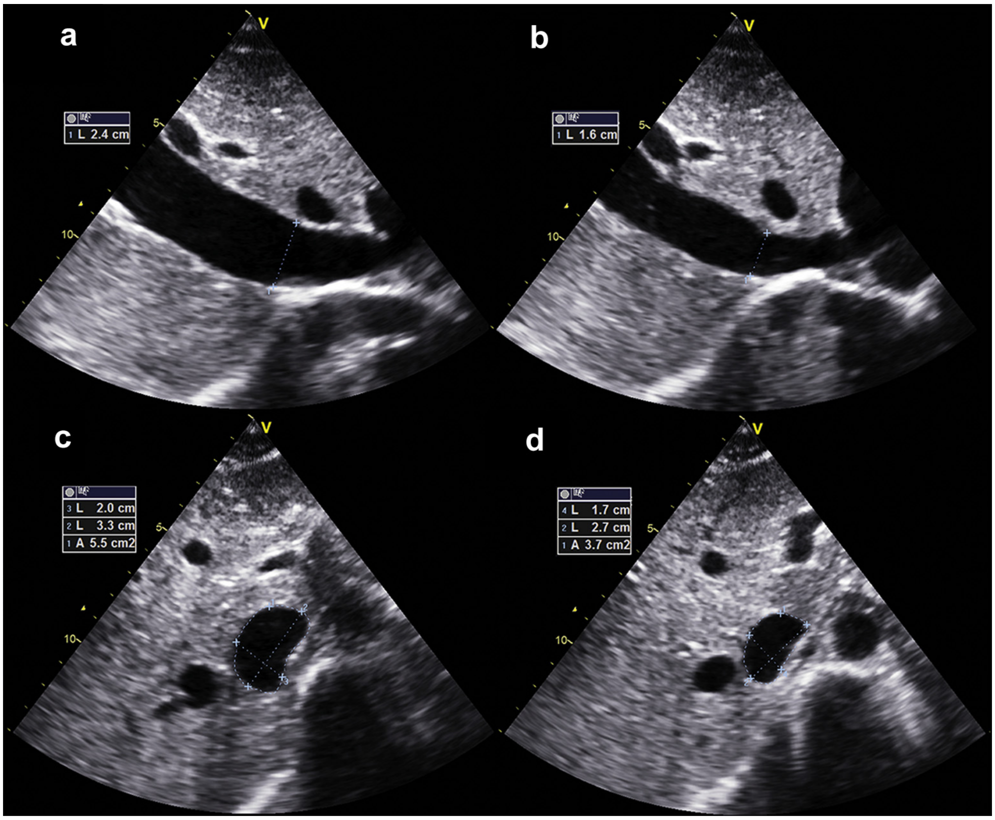

Fig. 1. Echocardiographic views of long-axis (a, b) and short-axis (c, d) maximal expiratory (a, c) and minimal inspiratory (b, d) inferior vena cava dimensions in one athlete.

and non-normally distributed continuous data were expressed as medians (25th–75th percentiles). Between-group differences were tested with Student's *t*-test or the Mann–Whitney *U*-test, whereas within-group differences were tested with a paired *t*-test or the Wilcoxon signed rank test. Frequencies were cross-tabulated and differences between groups were tested with the χ^2 test. Bivariate correlation analysis was performed to explore how $VO_{2\ max}$, LVEDV and RA area correlated to IVC dimensions, IVC shape and collapsibility. Differences were

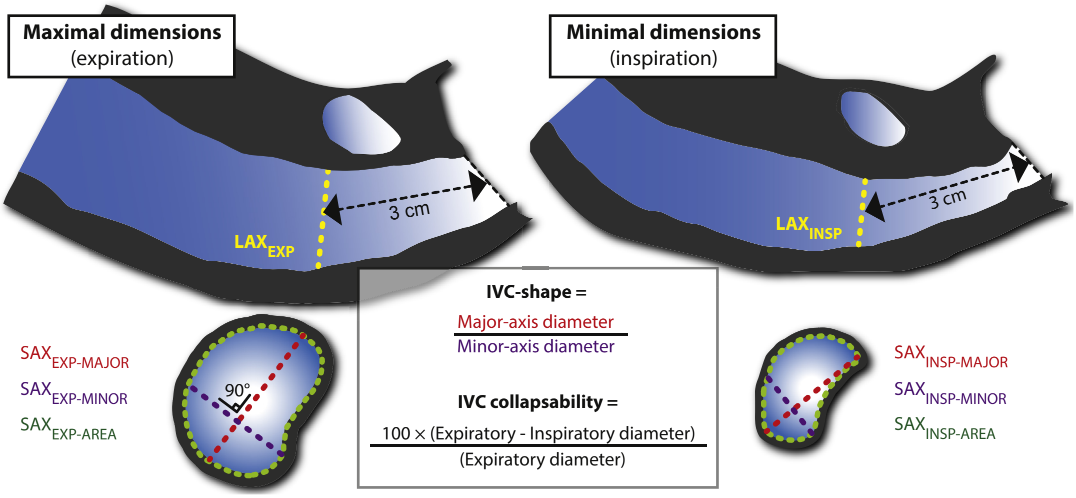

Fig. 2. Schematic of inferior vena cava measurements during expiration (left) and inspiration (right). Short-axis measurements obtained after a 90° rotation of the transducer approximate the level of diameter measurement in the long-axis view. Calculation of inferior vena cava shape is outlined in the box. IVC = inferior vena cava; LAX = long-axis; SAX = short-axis; EXP = expiration; INSP = inspiration.

tested two-sided, and a p value ≤ 0.05 was considered to indicate statistical significance. Results were analyzed using SPSS Statistics Version 22 (IBM, Armonk, NY, USA).

Inter- and intra-observer variability was tested in 16 randomly selected subjects for $SAX_{EXP\text{-}AREA}$ and four linear measures of IVC diameter. The coefficient of variation (% COV) was calculated as $\sqrt{(\sum d_i^2/2n)}$/(overall means), where d_i is the difference between the ith 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 intra-observer variability in an absolute agreement two-way mixed model.

RESULTS

Data quality and reproducibility

Image quality permitted long-axis measurements in 87 subjects (44 ATH); short-axis measurements were possible in 80 subjects (41 ATH). In total, 87% of 752 possible measurements could be obtained. Mean intra-observer variability (with ICC) for long-axis IVC diameter was 7.1% (0.91); for short-axis diameter 5.4% (0.92); and for $SAX_{EXP\text{-}AREA}$ 6.5% (0.95). Mean inter-observer variability (ICC) for long-axis IVC diameter was 9.9% (0.81); for short-axis diameter 10.5% (0.69); and for $SAX_{EXP\text{-}AREA}$ 13.7% (0.80).

Subject characteristics and standard echocardiographic measures

Mean age was similar for the two groups (both 21 ± 2 y, $p = 0.743$), whereas ATH were taller (1.68 ± 0.06 vs. 1.66 ± 0.05 m, $p = 0.028$) and had larger body surface area (1.69 ± 0.10 vs. 1.63 ± 0.09 m^2, $p = 0.008$) compared with CON. The cardiorespiratory conditioning of ATH was reflected in a lower heart rate at rest (54 ± 8 vs. 71 ± 10 beats/min, $p < 0.001$) and higher $VO_{2\ max}$ (52 ± 5 vs. 39 ± 5 mL/kg/min, $p < 0.001$) compared with values for 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 for 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 under Methods did not differ between trained and untrained subjects (χ^2, $p = 0.877$), nor did the proportion of subjects in dichotomized follicular and luteal categories (χ^2, $p = 0.463$).

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. 2015b). Absolute RA area was 39% larger in ATH (15.7 ± 2.7 vs. 11.3 ± 1.9 cm^2, $p < 0.001$), 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, on both expiration and inspiration (Table 1). LAX_{EXP} and LAX_{INSP} were 17% and 15% larger in ATH than in CON, respectively, whereas $SAX_{EXP\text{-}AREA}$ and $SAX_{INSP\text{-}AREA}$ were 17% and 27% larger in ATH than in CON. After indexing by the proper dimension of BSA, LAX_{EXP} was 14% larger and $SAX_{INSP\text{-}AREA}$ 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 on both inspiration and expiration (Fig. 3). Bland–Altman plots are provided in Supplementary Figure 1 (online only, available at http://dx.doi.org/10.1016/j.ultrasmedbio.2016.07.003).

Table 1. Absolute and indexed inferior vena cava measurements during expiration and inspiration

	Maximal dimension (expiration, mm)			Minimal dimension (inspiration, mm)		
Measurement	Athletes	Controls	p value	Athletes	Controls	p value
Absolute dimensions						
LAX diameter (mm)	24 ± 3 (19–31)	20 ± 3 (15–26)	<0.001	17 ± 5 (10–28)	15 ± 5 (7–23)	0.035
SAX major diameter (mm)	31 ± 5 (23–42)	29 ± 5 (21–38)	0.054	24 ± 5 (17–35)	22 ± 5 (12–30)	0.023
SAX minor diameter (mm)	23 ± 4 (16–32)	22 ± 4 (13–28)	0.155	18 ± 5 (10–25)	16 ± 5 (6–25)	0.052
SAX area (cm^2)	5.5 ± 1.5 (3.1–8.2)	4.7 ± 1.4 (2.4–7.4)	0.014	3.4 ± 1.4 (1.3–5.8)	2.7 ± 1.2 (0.5–5.0)	0.020
Dimensions indexed by body surface area*						
LAX diameter	18 ± 2 (15–23)	16 ± 3 (12–20)	<0.001	13 ± 4 (8–22)	12 ± 4 (6–18)	0.065
SAX major diameter	24 ± 4 (18–32)	22 ± 4 (16–29)	0.131	19 ± 4 (13–27)	17 ± 4 (9–23)	0.044
SAX minor diameter	18 ± 3 (12–25)	17 ± 3 (10–22)	0.280	14 ± 4 (8–19)	12 ± 4 (5–19)	0.092
SAX area	3.4 ± 1.4 (1.8–4.8)	2.7 ± 1.2 (1.5–4.8)	0.020	2.0 ± 0.9 (0.8–3.5)	1.6 ± 0.8 (0.3–3.0)	0.042

LAX = long-axis; SAX = short-axis.

Data are expressed as the mean ± standard deviation (5th–95th percentiles).

* Indexing by the proper dimension of body surface area, as described under Methods.

Both $SAX_{EXP\text{-}MAJOR}$ and $SAX_{INSP\text{-}MAJOR}$ were larger than the corresponding LAX diameters (both $p < 0.001$), whereas $SAX_{EXP\text{-}MINOR}$ and $SAX_{INSP\text{-}MINOR}$ were similar to the corresponding LAX diameters (both $p > 0.1$).

Inferior vena cava shape and inspiratory dimensional decrease. There were no statistically significant between-group differences in the inspiratory decrease in any IVC dimension. The IVC collapsibility index (*i.e.,* relative decrease in subcostal long-axis diameter) was 29 ± 15 versus 28 ± 17% in ATH and CON, respectively ($p = 0.785$), whereas 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 (Fig. 4). In the whole sample, IVC shape was similar at $SAX_{EXP\text{-}AREA}$, 1.3 (1.2–1.5), and $SAX_{INSP\text{-}AREA}$, 1.4 (1.2–1.6), $p = 0.054$. At $SAX_{EXP\text{-}AREA}$, only one control subject had a ratio >2.0 (2.1), whereas three controls and one athlete had a ratio >2.0 at $SAX_{INSP\text{-}AREA}$ (2.1–2.6).

Inferior vena cava correlations

In the whole sample of females, LAX_{EXP} was the IVC dimension that correlated most strongly to $VO_{2\ max}$ (Fig. 5), LVEDV and RA area. The correlations were moderate ($VO_{2\ max}$ $r = 0.52$, LVEDV $r = 0.46$, RA area $r = 0.49$, all $p < 0.001$). There was no correlation between $VO_{2\ max}$, LVEDV or RA area and IVC shape or relative decrease in IVC dimension.

The relative decrease in IVC long-axis diameter with inspiration correlated negatively with LAX_{EXP} ($r = -0.311$, $p < 0.03$) and the relative decrease in SAX area correlated negatively with $SAX_{EXP\text{-}AREA}$ ($r = -0.275$, $p < 0.014$).

DISCUSSION

IVC dimensions in trained versus untrained subjects

The most common measure of IVC dimension, recommended by current guidelines, is LAX_{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 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 (D'Ascenzi et al. 2013; Erol and Karakelleoglu 2002; Goldhammer et al. 1999; Zeppilli et al. 1995). The only study that explicitly reports *maximal* subcostal IVC long-axis diameter in trained subjects found male cyclists, long-distance runners and volleyball players to have mean IVC diameters of 28, 28 and 27 mm, respectively (Zeppilli et al.

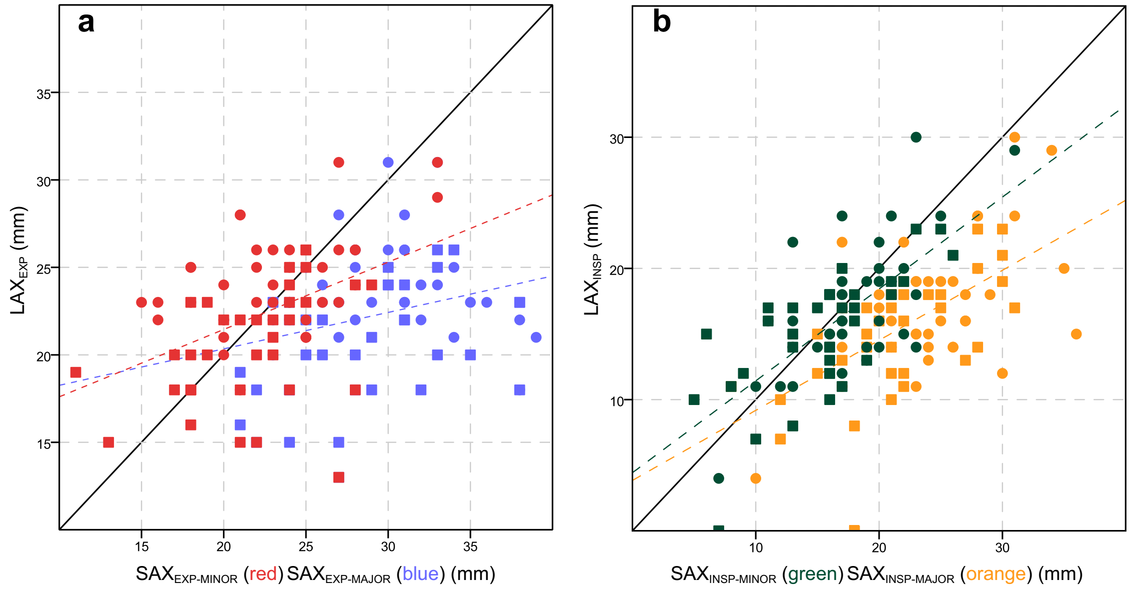

Fig. 3. (a) Plot of maximal diameters obtained during expiration in long-axis view (y-axis) against major- and minor-axis diameters from short-axis view (x-axis). (b) Corresponding minimal measures during inspiration. *Circles* represent trained females, and *squares* represent untrained females. Long-axis diameter corresponded more closely to short-axis minor diameter than major diameter at expiration as well as at inspiration. LAX = long-axis; EXP = expiration; SAX = short-axis; INSP = inspiration.

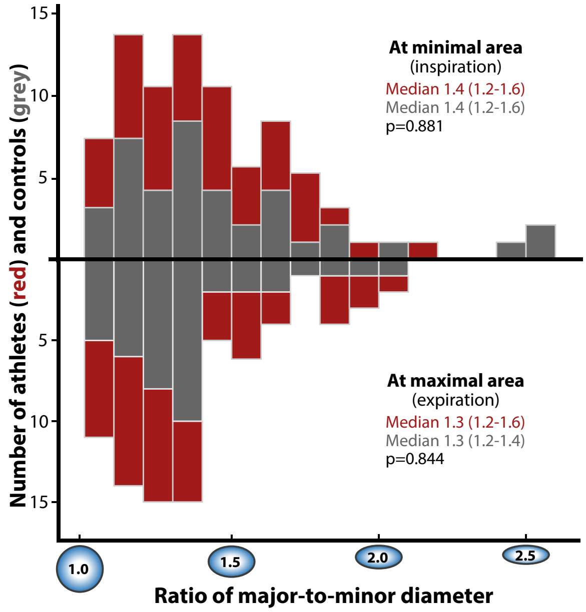

Fig. 4. Distribution of major-axis diameter to minor-axis diameter ratios (*i.e.,* shape) at maximal area during expiration (top) and minimal area during inspiration (bottom). *Red* and *gray* denote athletes and controls, respectively, with median values for the groups presented in the same color. A schematic of the corresponding ratio of a cylinder with constant width is provided on the x-axis. There were no between-group differences in the median value of inferior vena cava shape during either expiration or inspiration.

1995). Division of these measures by the square-rooted BSA of the subjects yielded indexed values of 20, 20 and 18 mm/m, respectively, with the corresponding value in our sample of female athletes being 18 ± 2 mm/m. Thus, although males have larger absolute IVC diameter, this difference would seem to be almost eradicated when accounting for body size.

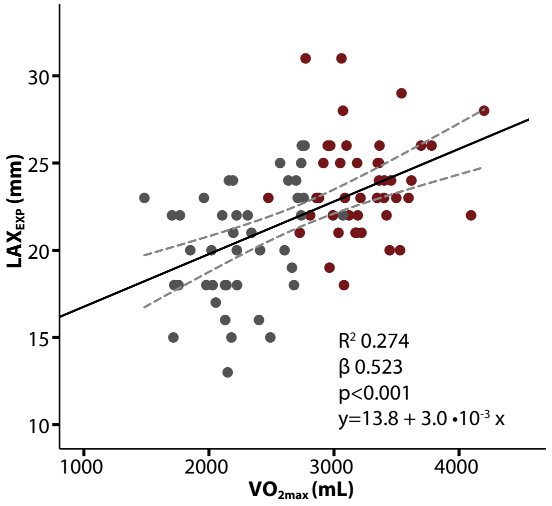

Fig. 5. Scatter-dot diagram with a linear regression line representing the relation between maximal inferior vena cava diameter measured in the long axis during expiration (LAX_{EXP}) and maximal oxygen uptake ($VO_{2\ max}$). *Red* and *gray* denote athletes and controls, respectively.

In a recent study by D'Ascenzi et al. (2014), IVC long-axis diameter in 24 professional female volleyball players increased from 17 to 21 mm (22%) after 16 wk 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 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. 2015b). When viewed together, current evidence indicates a substantial increase in IVC long-axis diameter after endurance training.

Influence of training on IVC dimensions: possible mechanisms

Blood flow in the IVC during submaximal supine cycling has been found to increase threefold at a workload at which 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 dilation of the arterial and cardiac chambers, respectively, through local endothelial factors (Green et al. 2012) and myocyte elongation caused by neurohumoral 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 underlying IVC dilation are distinct from other cardiovascular adaptions to endurance exercise. However, the mechanisms underlying chronic IVC dilation in endurance-trained athletes have not been established. Assuming RA pressure is similar in trained and untrained subjects (as discussed in the next subsection), other physiologic 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 an ~14% mean decrease in IVC maximal long-axis diameter accompanied by a 1.5% mean weight loss in 26 male American football players after a 3-h training session. 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) reported that 240 min of one-legged cycling per week for a 6-wk 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. 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 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 compared with 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 for 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 diameter to minor diameter at maximal area exceeded 2.0 in only one subject. These findings could be of interest as the role of IVC shape in the diagnosis of and prognosis for trauma patients (Johnson et al. 2013; Matsumoto et al. 2010), as well as hemodialysis patients (Naruse et al. 2007), is emerging. To our knowledge, however, normal IVC shape in healthy persons has not yet been determined.

The relative decrease in IVC dimension, imposed by the negative intra-thoracic pressure after 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, a dilated IVC was not associated with decreased IVC collapse in ATH compared with CON, which indicates similar RA pressures for the two groups and is supported by our finding of similar IVC shape for the two 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 with 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' ratios 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 using right atrial catheterization in eight young subjects with varying $VO_{2\ max}$ values (Stickland et al. 2006), as well as in a recent study including 102 elderly subjects with differences in lifelong exercise dose and current $VO_{2\ max}$ (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-axis versus short-axis measurements

An interesting finding was that LAX diameter corresponded more closely to SAX minor-axis than to major-axis diameter and that LAX measurements underestimated maximal IVC diameter during both expiration and inspiration (Fig. 3; Supplementary Fig. 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 Fig. 1). Our finding contrasts with Moreno et al. (1984), who found no difference between maximal LAX and SAX diameters in a mixed sample of cardiac patients and healthy subjects. However, the lack of data on IVC shape and the presence of right heart disease and elevated RA pressure in a substantial portion of the subjects 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 $VO_{2\ max}$, LVEDV and RA area

The IVC measurement correlating most strongly to $VO_{2\ max}$, LVEDV and RA area was LAX_{EXP}. We have previously reported stronger correlations between $VO_{2\ max}$ and LVEDV and RA area ($r = 0.71$ and $r = 0.64$, respectively) than found between $VO_{2\ max}$ and any measure of IVC size in the present study (Hedman et al. 2015b). This could imply that IVC dilation is secondary to systemic adaptations also affecting cardiac dimensions (and $VO_{2\ max}$), whereas cardiac dimensions have a more direct effect on $VO_{2\ max}$. This may be further supported by the observation that IVC dimension correlated similarly strongly to LVEDV and RA area as to VO_{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 level 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 contraceptives 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 dimensions, and this was beyond the scope of the present study. However, as there was no difference in the proportions 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 present study.

Limitations

First, we chose to measure long-axis IVC diameter 3 cm caudal to the junction with the RA so that we could measure LAX diameter at the same position as SAX diameter. This may impose a limitation in comparing our long-axis diameters with those from previous athlete–control studies, which applied a more cranial approach, often 1 to 2 cm 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 (Goldhammer et al. 1999; Zeppilli et al. 1995). This, however, would 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, whereas the IVC was similarly shaped and exhibited a similar relative decrease in dimensions with inspiration in both groups. The IVC dimensions correlated positively with $VO_{2\ max}$ and cardiac dimensions, suggesting increasing IVC dilation with increasing fitness, although the mechanisms underlying IVC dilation in trained athletes remains to be elucidated. Finally, we found that IVC diameter measured in the long-axis view underestimates the maximal IVC diameter and corresponds more closely to short-axis minor diameter.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.ultrasmedbio.2016.07.003.

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