Reference Values for and Determinants of Right Atrial Area in Healthy Adults by Two-Dimensional Echocardiography

Grünig et al: Reference Values of Right Atrial Area

Ekkehard Grünig, MD1*; Philipp Henn1*; Antonello D’Andrea, MD2*;
Martin Claussen, MD3; Nicola Ehlken, BSc1; Felicitas Maier1; Robert Naeije, MD, PhD4;
Christian Nagel, MD1; Felix Prange1; Johannes Weidenhammer1;
Christine Fischer, PhD5*; Eduardo Bossone, MD6*

*equally contributed

Centre for Pulmonary Hypertension at Thoraxklinik Heidelberg, Germany1; Second University of Naples, Monaldi Hospital, Naples, Italy2; Department of Pneumology, Clinic Grosshansdorf, Germany3; Erasme University Hospital Free University of Brussels, Brussels, Belgium4; Department of Human Genetics, University of Heidelberg, Germany5; Cardiology Division, "Cava de' Tirreni and Amalfi Coast" Hospital, Heart Dept., University of Salerno – Italy, and Cardiac Surgery Dept., IRCCS Policlinico San Donato, Milan, Italy6

Correspondence to
Ekkehard Grünig, MD
Centre for Pulmonary Hypertension Thoraxklinik
University Hospital Heidelberg
Amalienstrasse 5, 69126 Heidelberg
Phone: +49-6221-396-8053
Fax: +49-6221-396-1209
E-Mail: ekkehard.gruenig@thoraxklinik-heidelberg.de

DOI: 10.1161/CIRCIMAGING.112.978031

Journal Subject Codes: Cardiovascular imaging agents/Techniques, Echocardiography
Abstract

**Background**—Right atrial (RA) size is important in screening, diagnosis and follow-up assessment in patients with pulmonary hypertension. The objective of this paper was to define normal reference values for RA area by echocardiography in a large population of athletic versus sedentary healthy subjects.

**Methods and Results**—In the first part of the study 880 healthy adult subjects (mean age 28±6 years, 38% female, 395 top-level endurance athletes, 255 strength athletes and 230 non-athletes) were prospectively assessed. In the second part we performed a pooled analysis of all studies published between 1976 and 2011 describing RA area in healthy subjects (n=624). Statistical analysis included the calculation of 95% quantiles for defining cut-off values. Mean RA area in the 880 subjects was significantly larger in endurance athletes as compared to strength and non-athletes. RA area correlated significantly with age, gender, body surface and endurance training. In synopsis of both datasets 95% quantiles for RA-area in strength- and non-athletes were 15.2cm² (95% confidence interval 14.7-15.7cm²) in females and 16.2cm² (95% confidence interval 15.8-16.6cm²) in males.

**Conclusions**—To our knowledge, this is the largest data set to describe RA size in adult healthy subjects (aged below 50 years). Cut-off values for RA area were significantly different in females (15cm²) and males (16cm²). Age, gender, body surface area and high level endurance training were determinants of RA area.

**Key Words:** echocardiography, right atrium, reference values, pulmonary hypertension
Right atrial (RA) size is of clinical importance since it reflects right ventricular (RV) function and is strongly associated with clinical outcomes in many conditions as in pulmonary hypertension [1-3]. The normal RA is a thin, oval structure influencing RV-function as passive conduit to RV in early diastole. When the tricuspid valve is open, it acts as reservoir for systemic venous return, and fills the RV by active contraction during late diastole [4]. RA-contraction is responsible for up to 30% of normal RV output [5]. In healthy subjects short elevations of RV pressure lead to stretching and enlargement of the RA, resulting in, more reservoir volume. This mechanism has been identified to compensate short term right ventricular overload [6]. Chronic pulmonary hypertension is followed by enlargement and remodeling of the RA with hypertrophy and reduced contractility [7,8].

Echocardiography has become the most clinically relevant non-invasive diagnostic technique evaluating the right heart [9]. It can be used for screening, diagnosis and follow-up assessments in several diseases affecting the right heart as in cardiomyopathy and pulmonary hypertension [9-11]. For echocardiographic evaluation of the RA size, the right atrial area is easy to obtain and seems to be more reliable than to assess right atrial diameters or volume [11,12]. Volumetric quantification of the right atrium is challenging because many assumptions are required [11] and it is more difficult to perform within the daily clinical practice. However, there are limited data regarding the normal size of RV and RA [3,11,13]. Furthermore, echocardiographic views required for optimal evaluation of the right heart are less well standardized leading to inconsistent measurements of RV and RA size. The reference value given for mean RA area in the recommendations of the American Society of Echocardiography of 18cm² is not gender specific and based on few studies including 293 healthy subjects only. Therefore, the authors of the current American guidelines for echocardiography stated that their text has to be viewed as an incentive to refine the normal
values of the right heart [11]. Today, there are no reference values given for RA area/size indexed for body surface area (BSA), age, physical training status or gender in any guidelines [11].

The aim of this study was to analyze the dimensions of RA area first in a large prospectively assessed population of healthy adults and second in a pooled analysis of all previously reported studies including those which have not been taken into account in current guidelines. Thus, we aimed to confirm reference-values for RA area based on prospectively obtained data and analysis of previously reported ones. Furthermore, we wanted to identify determinants of RA size such as gender, age, BSA and exercise training status.

Methods

Study population

From June 2008 to March 2009, 880 healthy athletic and non-athletic subjects were prospectively and consecutively studied by 2-D-echocardiography at Monaldi Hospital, Naples, Italy as previously described [14]. The athletes were employed by professional sports associations and had been trained intensively 15 to 20 h/week for >4 years. The subjects were referred for cardiovascular pre-participation screening. Volunteer controls were all recruited in Naples (Italy), selected from the department of Cardiology and investigated for work eligibility. None of the control subjects had cardiovascular structural or functional abnormalities or received any medication. All subjects underwent a detailed history, physical examination, body surface area, ECG, chest radiography, an exercise test, and comprehensive transthoracic echocardiography, including Doppler studies as described previously [14]. Subjects with cardiopulmonary diseases such as coronary artery disease, systemic arterial hypertension, valvular or congenital heart disease, bicuspid aortic valve, congestive heart failure, cardiomyopathies, and diabetes mellitus were excluded. Additional exclusion criteria
were sinus tachycardia and inadequate echocardiographic image quality. Use of anabolic steroids or other illicit drugs was ruled out by medical history and patient interview. According to these criteria, 10 subjects were excluded (3 for bicuspid aortic valve, 1 for hypertrophic cardiomyopathy, 4 for use of anabolic steroids, and 2 for inadequate echocardiographic image quality. The final study population consisted of 880 subjects. Whereas results for healthy non-athletes have not been analyzed yet, some data of the right heart function in athletes have been reported previously [14]. The study was approved by the local Ethics Committee. All subjects enrolled in the study gave informed consent.

Echocardiographic assessment

Two-dimensional and Doppler-echocardiographic recordings were performed using 2.5 MHz Duplex probes and conventional equipment (Vivid 7, GE Healthcare, Milwaukee, Wisconsin) by experienced cardiac sonographers. RA measurements were assessed in the apical 4-chamber view. RA area was estimated by planimetry at the end of ventricular systole (largest volume), tracing from the lateral aspect of the tricuspid annulus to the septal aspect, excluding the area between the leaflets and annulus, following the RA endocardium (Figure 1). All studies were reviewed and analysed off-line by two independent observers blinded to the clinical characteristics of the study population. As an example Figure 1 shows a normal and enlarged RA area measured by echocardiography and describes the technique. For exclusion of pulmonary hypertension or any heart diseases possibly affecting the right heart size as congenital heart defects, a complete echocardiographic assessment including assessment of pulmonary artery pressures was performed in all subjects [15]. For all calculations the mean value of at least 3-5 measurements was used. RA pressure was estimated from characteristics of the inferior vena cava [16]. Patients with suspected heart
diseases or elevated pulmonary systolic artery pressures (>35mmHg) and/or elevated estimated RA-pressure (diameter of inferior vena cava >20mm) were excluded.

**Literature search**
We performed a systematic literature search using Medline and Cochrane Database for studies published between January 1966 and October 2011 reporting echocardiographic RA-measurements in healthy subjects. This encompassed studies reporting normal reference values in humans. Our approach was to search by Medical Subheadings (MeSH) or key words related to RA size, diameters, volume and area. In addition, reference lists of relevant studies, practice guidelines and reviews were screened to identify further studies not detected by the electronic search. All studies in English, German and Italian language were screened. We selected studies that described RA size/area in healthy adults without cardiovascular diseases using standardized echocardiographic views. We excluded studies with unclear echocardiographic techniques or status of subjects.

**Statistical methods**
All analyses were performed by a statistician (CF).

**Determination of RA area and RA area indexed for BSA:** In the prospective analysis all reported values of RA area represent the mean of at least three measurements. In order to calculate RA area indexed for body surface area (BSA) in the prospective study, we used the formula: RA area indexed for BSA [cm²/m²] = RA area absolute [cm²] / BSA [m²] for each individual measurement. BSA was calculated using the formula BSA= weight [kg] ^0.425 * height [cm] * 71.84*10^-4 [17]. If only RA area absolute or RA area indexed was presented in the literature, we calculated the other value using the mean BSA if possible (see Table 1).
**Prospective analysis:** RA areas are presented as means and standard deviations. As upper cut-off values for normal RA-areas for females and males we used 95% quantiles and their 95% confidence intervals. The values were calculated with and without assuming a normal distribution using SAS V.9.2 (SAS Institute Inc., Cary, NC, USA). The calculation assuming non-normally distributed values led to nearly identical quantiles and confidence intervals, therefore we present the results assuming normality. The comparison of 95% quantiles between male and female and between groups with different exercise training status was performed using the SAS QUANTREG procedure.

**Analysis of determinants:** We calculated correlation coefficients to describe determinants of RA area. Additionally, groups with different exercise training status (as endurance-exercise training, strength-exercise training or non-athletes) or gender groups were compared by analysis of variance (ANOVA). Multivariate regression analysis was performed to take age, BSA and sex simultaneously into account. P-values <0.05 were considered statistically significant.

For these analyses we used IBM SPSS 20 (SPSS Statistics V.20, IBM Corporation, Somers, New York).

**Literature analysis:** Since in the literature only aggregated data, namely means, standard deviations and sample sizes are given, we estimated the 95% percentile assuming normally distributed data. Additionally, 95% confidence intervals for the 95% percentile were determined by using the 97.5% confidence intervals of the estimated mean and standard deviation of each single study. We combined the results from the literature with our data by pooling means and standard deviations for each study weighted by sample size assuming a common underlying normal distribution. Based on the pooled mean and the pooled standard deviation the 95% percentiles and their 95% confidence intervals were estimated as described above.
To analyze the influence of single studies on the pooled estimate a sensitivity analysis was performed by leaving out one study after the other and calculating the pooled estimates with the remaining studies. All these analyses were performed with tailored software.

Results

RA area prospectively obtained in healthy athletes/non-athletes

We prospectively assessed 880 healthy adults: 230 non-athletes, 255 strength athletes and 395 endurance athletes (Table 1, Figure 2, Figure 3). Mean age was 28.2±10.5 (from 18-45) years and did not significantly differ between groups. Mean absolute and indexed RA area values with standard deviation, the 95% quantiles and range of confidence intervals are shown in Table 1. The 95% quantiles which have been defined as cut-off values for normal RA area were almost identical in non-athletes and strength-athletes. In non-athletes the 95% quantiles were significantly different between male and female (p=0.0042) with 15.1 cm² (CI 14.3-16.0 cm²) in females, 15.7 cm² (CI 15.1-16.5 cm²) in males and 15.5 cm² (CI 15.1-15.9 cm²) in mixed gender (Table 1). RA area indexed for BSA in non-athletes was 8.2 cm²/m² in females, 8.4 cm²/m² in males and 8.3 cm²/m² in the mixed gender group (Table 1).

Correlation analysis of RA area with age, gender, body surface area and exercise training status

RA area means were significantly different between non-athletes (12.5±2.0 cm²), strength athletes (12.7±1.6 cm²) and endurance athletes (15.4±2.1 cm², p<0.0001, ANOVA, figure 2a) and between males and females of the non-athletic group (p=0.0042, Figure 2b). If gender, age, BSA and training-status were taken into account simultaneously, only the correlation of RA area with endurance-training and BSA but not gender remained significant. There was a significant but weak correlation of RA area with age (r=0.17, p<0.0001) and BSA (r=0.33,
p<0.0001) in non-athletes + strength athletes (n=485). In endurance athletes (n=395) a weak correlation between RA area and Age (r=0.23, p<0.001) and between RA area and BSA (r=0.29, p<0.001) occurred respectively. Only 3% of the variability of RA area could be explained by age, 11% by BSA.

The different RA area in males and females was confirmed in the pooled analysis of those previously published studies which distinguished between genders. In all of these studies [18, 19, 21] we found significantly different mean RA areas in males and females, ranging from 2.6 to 3.0 cm². In publications selected for the pooled analysis we could not perform further correlation analysis concerning age, training status and BSA or any other variables because only mean values for RA area and no analysis for determinants had been reported.

**RA area obtained by pooled analysis of previously published studies.**

Eleven studies were detected by screening of medline- and cochrane-databases for right atrial size. Two of the 11 studies were excluded [2, 26]. The second oldest of the 11 studies from Reeves et al. 1981 identified a mean value of RA area of 16.1±3.4 cm² in a gender-mixed cohort of 21 healthy controls. However, they used a sector-scan echocardiography Picker 80-C cardiac imager which was technically very limited; echocardiographic 4-chamber views were different [26]. The data of Raymond [2] were not included because the RA area index was calculated using height instead of BSA. Therefore, we were unable to calculate the absolute or indexed values for RA area as no mean height was provided.

Thus, nine studies published between 1979 and 2011 with 624 healthy subjects were used for the pooled analysis (Table 2). The assessed subjects had been classified as “healthy” and “free of heart disease” in all studies. As far as specified, most studies had performed electrocardiograms and physical examinations to exclude any heart disease. In one study right- and left heart catheterization has been performed [26]. In this study also rubber casts
fashioned from the right heart chambers during necropsy have been assessed in 8 deceased subjects without clinical or anatomical evidence of heart-lung diseases to validate the echocardiographic dimensions of the heart chambers [22]. Overall, the assessed subjects aged between 18-70 years, the mean age ranged between 22.2±4.5 years [21] and 45 years [22] (Table 2). Most subjects had been younger than 50 years of age. The sample size ranged from 11 to 219 subjects/study. Percentage of females ranged from 27 to 54.3% while one study did not mention gender distribution (Table 2). Three studies were retrospective in design, in 3 others the study design was not completely clear; 5 studies [12,18-20] were designed for reference value determination and four studies [21,22-25] used healthy subjects as control group.

Table 3 summarizes the mean values for absolute and indexed RA area, standard deviation, 95% quantiles and their 95% confidence intervals for all studies used in the pooled analysis and for our study population. Furthermore, in each of the identified studies RA values obtained in the subgroups "gender" and "training-status" are shown. The mean absolute RA area ranged from 4 cm² [23], (which we considered as implausible and therefore excluded the values from further calculation), 6.6 cm² [19] in female non-athletes to 21.2 cm² [21] in male endurance-athletes. In each study values for the 95% quantiles and confidence intervals were calculated and compared with the values we obtained in our study population in 880 healthy subjects [14].

**Pooled values for RA area derived from 10 studies: pooled analysis of previous data and prospectively assessed healthy subjects**

In the heading lines (grey indicated) of table 3 mean values are given for in total 378 male, 260 female, 1012 unknown gender non-athletes and strength athletes, respectively; 305 male and 170 female endurance athletes. We included non-athletes and strength athletes in the
normal group since their RA distributions are very similar. The means derived from values of
the 9 studies of the pooled analysis and our own prospective data of 880 healthy subjects.
Figure 3 illustrates the 95% quantiles and confidence intervals of RA area assigned to the
analyzed studies and subgroups. Overall, in non-/strength athletes pooled mean RA area was
12.2±1.8 cm² in females, 13.0±1.9 cm² in males, and 12.6±3.0 cm² in the mixed gender group
(Table 3). Pooled 95% quantiles of RA area were 15.2 cm² in females, 16.2 cm² in males and
17.5 cm² in mixed gender (Table 3, figure 3). Pooled 95% quantiles of RA areas indexed for
BSA were 8.5 (8.3-8.8) cm²/m² in females, 8.6 (8.4-8.8) cm²/m² in males, 10.1 (9.9-10.4)
cm²/m² in the mixed gender group.

Sensitivity analysis
Without our prospectively obtained data the references values for mixed gender were slightly
higher and without Kelly et al. [25] they were slightly lower (16.7 cm²). For females no study
had a remarkable influence. The leave-one-out estimates for the reference values for males
varied between 15.9-18.3 cm².

Discussion
To the best of our knowledge, this is the largest data set on RA size in healthy adults (n=880
our study population, n=624 pooled analysis) aged between 18 and 70 years (most of them
aged below 50 years) up to now. The calculated reference values for RA size obtained by 2-
D-echocardiography in apical 4-chamber view are based on almost all prospective and
retrospective studies which have been published so far. This is the first study providing
normal reference values for RA area. The study confirms that absolute cut-off values should
be determined and used gender-specifically. Absolute cut-off values for RA area in non-
athletes/strength athletes were significantly different in females (15 cm²) and males (16 cm²),
whereas values indexed for BSA were similar in both gender (females 8.5 cm²/m²; males 8.6 cm²/m²). Age, gender, body surface area and high level endurance-exercise training were identified as determinants of RA area. Top-level endurance-athletes did exceed the reference values of RA area for non-athletes and strength athletes and showed no significant differences between males and females.

RA size evaluated by 2-D-echocardiography correlated well with rubber heart chamber casts obtained at autopsy [22], with hemodynamic measurements and with assessment by Magnetic Resonance Imaging [27]. The absolute RA area obtained by echocardiography in the apical 4-chamber-view is a reliable and in most subjects’ accurately measurable parameter. It can be obtained even by older echocardiography devices and is of major clinical relevance. This parameter reflects RV-function [5,8] and is important for follow-up assessment and risk-stratification in patients with right heart failure as in patients with pulmonary hypertension [9,10]. Furthermore, enlarged RA-area belongs to the echocardiographic parameters which might raise or reinforce suspicion of pulmonary hypertension independently of tricuspid regurgitation velocity [9,10] and may be an early indicator for primary diseases of the right heart. RA area distinguished normal subjects from patients with right ventricular volume overload or right heart diseases with only minimal overlap between the groups [8,22,23,25] as long as correct cut-off values were used. Furthermore, enlarged atrial size may be an early indicator for pulmonary hypertension and/or primary diseases of the right heart.

For clinical practice it is more convenient to measure the absolute area instead of performing the corrections for body surface area. Therefore, the finding that females and males have significantly different absolute RA areas is of clinical importance and has already been observed in small cohorts of healthy subjects [18-20]. Nevertheless, gender differences in RA size have not been analyzed systematically so far and have not led to different gender specific reference values [11]. This study confirms for the first time gender differences and the
influence of age, BSA and training-status on echocardiographic RA-area in a large number of healthy adult subjects. Mixed gender values for absolute RA area [11] should therefore not be used any longer to avoid the risk of underestimation of RA enlargement especially in women. However, no significant gender differences had been observed when RA area was corrected for BSA and training status (endurance-athletes). Different reference values for males and females have also been documented for echocardiographic right ventricular end-diastolic area [28].

Absolute RA area was significantly but weakly correlated with age. Subjects with older age had slightly enlarged RA areas. However, most subjects of this study were less than 50 years of age. In this cohort, age accounted for only 3% of variance of values. According to the results of the prospective study and the pooled analysis of all previous studies there is no need to adapt the reference values of 15 cm² for females and 16 cm² for males to age. Nevertheless, further evaluation of children and healthy subjects >50 years is necessary to determine normal RA area in these groups.

Numerous studies have described “athletes heart syndrome” with chamber enlargements of the left and right heart [29]. However the effect on RA size is less well evaluated. Acute, transient RA and right ventricular dilatation, reduction of right ventricular ejection fraction obtained by magnetic resonance imaging, release of B-type natriuretic peptides [30] and of cardiac troponin I [31] were seen immediately after severe endurance exercise as Marathon running. Ector et al. proposed that the right ventricle may be more severely affected by endurance training due to its thin-walled structure than the left ventricle [32]. Enlarged RA size compared to sedentary controls by 2-D-echocardiography was also described in professional tennis players participating at the French open [21]. In our study endurance-trained top-level athletes had substantially larger RA areas with a 95% quantile of 19.5 cm² than measured in non-athletes and strength-athletes. A possible explanation for this might be
that endurance training leads to higher volume loads of the right ventricle [29,33], whereas strength-athletes generate higher pressures with only transiently increased volume loads [29,33].

**Limitations**

The studies included for pooled analysis had a different quality of defining “healthy participants”. Only in one study right- and left heart catheterization has been performed [22]. Some other studies were retrospective in design and not all studies aimed to determine reference values so that we cannot exclude a referral bias. These studies caused a larger standard deviation of mean RA-areas which has also been reflected in the larger 95% percentile for mixed gender in the pooled analysis compared to the values obtained in the prospective study. However, the strength of this paper is that the values for RA area selected for pooled analysis have been compared with data which have been prospectively assessed. The prospective examinations used actual standards in the definition of healthy subjects and avoided referral bias by the assessment of subjects who ask for a job-certificate. If we would have referred to the prospective study only, reference values for absolute RA area would rather be slightly smaller than 15 cm² in females and 16 cm² in males.

The majority of subjects analyzed in the prospective study and in the pooled analysis were of young age (<45 years). There is a lack of data describing RA area in children or subjects >50 years. In subjects of older age the definition of “healthy” would need a detailed diagnostic work up including right- and left heart catheterization. However, the findings in the study of Bommer et al. [22] indicate that RA area in subjects of older age do not significantly exceed the reference values confirmed in this study.

Only few studies have been excluded from this pooled analysis. Their values obtained for RA-area would not have changed the reference values obtained in the analysis. We chose the 95% quantiles as normal reference values since the 5% largest values may indicate
pathological processes. Another quantile as 97.5% could have been considered but would have changed the resulted reference values only slightly.

**Conclusion**

To our knowledge, this is the largest data set to describe RA size in adult healthy subjects (aged below 50 years). Cut-off values for RA area were significantly different in females (15cm²) and males (16cm²) and should therefore be used gender specific in future. Age, gender, body surface area and high level endurance training were determinants of RA area. Further studies in children and subjects aged >50 years are needed.

**Disclosures**

None.

**References**


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Table 1. Characteristics of for pooled analysis selected studies on RA-area by 2-D-echocardiography

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>n</th>
<th>retrospective study design</th>
<th>% female</th>
<th>BSA</th>
<th>gender distinction</th>
<th>Area abs.</th>
<th>Index</th>
<th>athletes</th>
<th>non-athletes</th>
<th>mean age (years)</th>
<th>mean age (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bommer et al. (22)</td>
<td>1979</td>
<td>25</td>
<td>x</td>
<td>44</td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>Cacho et al. (23)</td>
<td>1983</td>
<td>11</td>
<td>x</td>
<td>27</td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td>22-37</td>
<td></td>
</tr>
<tr>
<td>Lambertz et al. (19)</td>
<td>1984</td>
<td>30</td>
<td>?</td>
<td>50</td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td>31 ± 10</td>
<td>28 ± 8</td>
</tr>
<tr>
<td>Triulzi et al. (12)</td>
<td>1984</td>
<td>67</td>
<td>?</td>
<td>?</td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>Wang et al. (20)</td>
<td>1984</td>
<td>54</td>
<td>46.3</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td>38.4</td>
<td>37.6</td>
</tr>
<tr>
<td>Lambertz et al. (18)</td>
<td>1986</td>
<td>43</td>
<td>?</td>
<td>51.2</td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td>40 ± 14</td>
<td>36 ± 14</td>
</tr>
<tr>
<td>Mansencal et al. (21)</td>
<td>2007</td>
<td>160</td>
<td>37.5</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td>24.9 ± 4.4</td>
<td>22.2 ± 4.5</td>
</tr>
<tr>
<td>Huez et al. (24)</td>
<td>2009</td>
<td>15</td>
<td>53</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td>36</td>
<td>12</td>
</tr>
<tr>
<td>Kelly et al. (25)</td>
<td>2010</td>
<td>219</td>
<td>x</td>
<td>54.3</td>
<td></td>
<td>X</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td>29.7 ± 25.2</td>
<td></td>
</tr>
<tr>
<td>sum</td>
<td></td>
<td>624</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

abs.= absolute, BSA= Body surface area; studies are listed in chronologic order of publication year.
Table 2. Right atrial (RA) area prospectively obtained in 880 healthy subjects

<table>
<thead>
<tr>
<th>gender</th>
<th>non-athletes</th>
<th>strength athletes</th>
<th>endurance athletes</th>
</tr>
</thead>
<tbody>
<tr>
<td>number</td>
<td>male</td>
<td>137 (15.6%)</td>
<td>155 (17.6%)</td>
</tr>
<tr>
<td>(% of total)</td>
<td>female</td>
<td>93 (10.6%)</td>
<td>100 (11.4%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>RA AREA [cm²]</th>
<th>mean ± SD</th>
<th>male</th>
<th>12.5 ± 2.0</th>
<th>12.7 ± 1.6</th>
<th>15.4 ± 2.1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q-95 (CI)</td>
<td></td>
<td></td>
<td>15.7 (15.1-16.5)</td>
<td>15.3 (14.8-15.9)</td>
<td>19.5 (19.0-20.0)</td>
</tr>
</tbody>
</table>

| mean ± SD | female | 11.9 ± 1.9 | 12.8 ± 1.5 | 15.3 ± 2.1 |
| Q-95 (CI) |         | 15.1 (14.3-16.0) | 15.3 (14.7-16.0) | 19.5 (18.5-20.5) |
| Q-95 (CI) | mixed   | 15.5 (15.1-15.9) | 15.5 (15.0-15.6) | 19.5 (19.0-20.0) |

<table>
<thead>
<tr>
<th>RA AREA INDEX [cm²/m²]</th>
<th>mean ± SD</th>
<th>male</th>
<th>6.7 ± 1.0</th>
<th>6.9 ± 0.9</th>
<th>8.3 ± 1.1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q-95 (CI)</td>
<td></td>
<td></td>
<td>8.4 (8.1-8.8)</td>
<td>8.3 (8.0-8.6)</td>
<td>10.4 (10.1-11.0)</td>
</tr>
</tbody>
</table>

| mean ± SD | female | 6.5 ± 1.0 | 7.0 ± 0.8 | 8.2 ± 1.1 |
| Q-95 (CI) |         | 8.2 (7.7-8.6) | 8.3 (8.0-8.6) | 10.4 (9.9-11.1) |
| Q-95 (CI) | mixed   | 8.3 (8.1-8.5) | 8.2 (8.1-8.5) | 10.4 (10.1-10.7) |

RA: right atrial, SD: standard deviation, Q-95: 95% quantile, CI: 95% confidence interval
Table 3. Mean absolute and for BSA indexed RA area: pooled values of our (D’Andrea) and for pooled analysis selected studies

<table>
<thead>
<tr>
<th></th>
<th>RA AREA [cm²]</th>
<th>RA AREA index [cm² / m²]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NON-ATHLETES</td>
<td>378</td>
<td>13.0±1.9</td>
</tr>
<tr>
<td>Lambertz 1984 non-athletes</td>
<td>15</td>
<td>13.6±4.7</td>
</tr>
<tr>
<td>Lambertz 1986 non-athletes</td>
<td>21</td>
<td>14.0±2.3</td>
</tr>
<tr>
<td>Mansencal non-athletes</td>
<td>50</td>
<td>14.9±1.7</td>
</tr>
<tr>
<td>D’Andrea non-athletes</td>
<td>137</td>
<td>12.5±2.0</td>
</tr>
<tr>
<td>D’Andrea strength</td>
<td>155</td>
<td>12.7±1.6</td>
</tr>
<tr>
<td>Male ENDURANCE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D’Andrea endurance</td>
<td>255</td>
<td>15.4±2.1</td>
</tr>
<tr>
<td>Mansencal endurance</td>
<td>50</td>
<td>21.2±4.0</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NON-ATHLETES</td>
<td>260</td>
<td>12.2±1.8</td>
</tr>
<tr>
<td>Lambertz 1984 non-athletes</td>
<td>15</td>
<td>10.6±2.8</td>
</tr>
<tr>
<td>Lambertz 1986 non-athletes</td>
<td>22</td>
<td>11.4±1.6</td>
</tr>
<tr>
<td>Mansencal non-athletes</td>
<td>30</td>
<td>12.2±2.4</td>
</tr>
<tr>
<td>D’Andrea non-athletes</td>
<td>93</td>
<td>11.9±1.9</td>
</tr>
<tr>
<td>D’Andrea strength</td>
<td>100</td>
<td>12.8±1.5</td>
</tr>
<tr>
<td>Female ENDURANCE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D’Andrea endurance</td>
<td>140</td>
<td>15.3±2.1</td>
</tr>
<tr>
<td>Mansencal endurance</td>
<td>30</td>
<td>16.1±3.6</td>
</tr>
<tr>
<td>Mixed Sex NON-ATHLETES</td>
<td>1012</td>
<td>12.6±3.0</td>
</tr>
</tbody>
</table>

| Bommer non-athletes      | 25  | 13.9±0.7 | 15.1 | 14.5-15.8 |    |       |     |           |
| Cacho non-athletes       | 11  | 7.1±0.6  | 8.0  | 7.4-9.1   | 11  | 4.0±0.3 | 4.5  | 4.2-5.1  |
| Triulzi non-athletes     | 67  | 13.5±2.0 | 16.8 | 15.8-17.9 | 67  | 7.7±1.1 | 9.6  | 9.0-10.3 |
| Wang non-athletes        | 48  | 13.0±3.0 | 17.9 | 16.3-20.0 | 48  | 7.1±1.6 | 9.8  | 8.9-10.9 |
| Huez non-athletes        | 15  | 15.0±7.0 | 26.5 | 19.9-36.7 | 15  | 8.3±3.9 | 14.7 | 11.0-20.4 |
| Kelly non-athletes       | 219 | 11.5±5.0 | 19.7 | 18.4-21.2 | 219 | 7.4±3.2 | 12.6 | 11.8-13.6 |

SD: standard deviation, Q-95: 95% quantile, L-CI/U-CI: lower and upper 95% confidence interval, Q-95: 95% quantile, RA: right atrial analysis for pooled values does not include endurance athletes.
Figure Legends

Figure 1. Echocardiographic measurement of RA-area in the apical 4-chamber view
The figure shows schematically and in echocardiographic pictures how RA area measurements have been performed in the apical 4-chamber view. On the left side, RA area is of normal size, the picture on the right side shows an enlarged RA area in a patient with pulmonary arterial hypertension.

Figure 2. Determinants of RA-area A: Type of training, B: Gender
2A: The whisker plot illustrates the effect of endurance and strength training on RA area, prospectively evaluated. Endurance athletes had significantly larger RA areas than non-athletes and strength athletes. 3B: This figure shows significantly different RA area sizes in male and female non-athletes. The boxes represent the values of all subjects in between 25% and 75% quantiles, median line, while the range from 5%-95% quantiles is displayed by the whiskers.

Figure 3. Mean values of echocardiographically measured RA area: in our data and for pooled analysis selected previous studies
The figure presents the 95% quantile of the RA area and the range of 95% confidence interval of our prospective data and previous publications selected for pooled analysis. The values are given for males and females with different training-status. At the bottom the pooled values are shown.
A. RA areas in different types of training

- Non-Athletes: n=230
- Strength Athletes: n=255
- Endurance Athletes: n=395

p<0.0001

B. RA areas in males and females of Non-Athletes

- Male: n=137
- Female: n=93

p=0.0042