Reference Values for and Determinants of Right Atrial Area in Healthy Adults by 2-Dimensional Echocardiography

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Methods and Results—In the first part of the study, 880 healthy adult subjects (mean age, 28±6 years; 38% women; 395 top-level endurance athletes, 255 strength athletes, and 230 nonathletes) 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 cutoff values. Mean RA area in the 880 subjects was significantly larger in endurance athletes compared with the strength athletes and nonathletes. RA area correlated significantly with age, sex, body surface, and endurance training. In a synopsis of both data sets, 95% quantiles for RA area in strength athletes and nonathletes were 15.2 cm² (95% confidence interval, 14.7–15.7) in women and 16.2 cm² (95% confidence interval, 15.8–16.6) in men.

Conclusions—To the best of our knowledge, this is the largest data set to describe RA size in adult healthy subjects (age <50 years). Cutoff values for RA area were significantly different in women (15 cm²) and men (16 cm²). Age, sex, body surface area, and high-level endurance training were determinants of RA area. (Circ Cardiovasc Imaging. 2013;6:117-124.)

Key Words: echocardiography ■ pulmonary hypertension ■ reference values ■ right atrium ■ risk factors

Right atrial (RA) size is of clinical importance because it reflects right ventricular (RV) function and is strongly associated with clinical outcomes in many conditions such as pulmonary hypertension.1-3 The normal RA is a thin, oval structure influencing RV function as a passive conduit to the RV in early diastole. When the tricuspid valve is open, it acts as a 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 for short-term RV overload.6 Chronic pulmonary hypertension is followed by enlargement and remodeling of the RA with hypertrophy and reduced contractility.7,8

Clinical Perspective on p 124

Echocardiography has become the most clinically relevant noninvasive diagnostic technique evaluating the right heart.9 It can be used for screening, diagnosis, and follow-up assessments in several diseases affecting the right side of the heart such as cardiomyopathy and pulmonary hypertension.9-11 For echocardiographic evaluation of the RA size, the RA area is easy to obtain and seems to be more reliable assessing RA diameters or volume.11,12 Volumetric quantification of the right atrium is challenging because many assumptions are required11 and it is more difficult to perform in the daily clinical practice. However, there are limited data on the normal size of the 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 18 cm² is not sex specific and is based on few studies including only 293 healthy subjects. 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 sex 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 that have not been taken into account in the current guidelines. Thus, we aimed to confirm reference values for RA area using prospectively obtained data and analyzing previously reported data. Furthermore, we wanted to identify determinants of RA size such as sex, age, BSA, and exercise training status.

Methods

Study Population
From June 2008 to March 2009, 880 healthy athletic and nonathletic subjects were prospectively and consecutively studied by 2-dimensional echocardiography at Monaldi Hospital, Naples, Italy, as previously described. The athletes were employed by professional sports associations and had been trained intensively 15 to 20 h/wk for >4 years. The subjects were referred for cardiovascular preparticipation screening. Volunteer control subjects 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, BSA, ECG, chest radiography, exercise test, and comprehensive transthoracic echocardiography, including Doppler studies, as described previously. 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. Although results for healthy nonathletes have not been analyzed yet, some data on the function of the right side of the heart in athletes have been reported previously. The study was approved by the local Ethics Committee. All subjects enrolled in the study gave informed consent.

Echocardiographic Assessment
Doppler and 2-dimensional echocardiographic recordings were performed with 2.5-MHz Duplex probes and conventional equipment (Vivid 7, GE Healthcare, Milwaukee, WI) by experienced cardiologists. 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, after the RA endocardium (Figure 1). All studies were reviewed and analyzed offline by 2 independent observers blinded to the clinical characteristics of the study population. As an example, Figure 1 shows a normal and an enlarged RA area measured by echocardiography and describes the technique. For exclusion of pulmonary hypertension or any heart diseases possibly affecting the size of the right side of the heart such as congenital heart defects, a complete echocardiographic assessment, including assessment of pulmonary artery pressures, was performed in all subjects. For all calculations, the mean value from at least 3 to 5 measurements was used. RA pressure was estimated from characteristics of the inferior vena cava. Patients with suspected heart diseases or elevated pulmonary systolic artery pressures (>35 mm Hg) and elevated estimated RA pressure (diameter of inferior vena cava >20 mm) were excluded.

Literature Search
We performed a systematic literature search using Medline and the 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 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 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 (C.F.).

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 3 measurements. To calculate RA area indexed for BSA in the prospective study, we used the following formula: RA area indexed for BSA (cm²/m²)=RA area absolute (cm²)/BSA (m²) for each individual measurement. RA was calculated using this formula: BSA=weight (kg)×0.425×height (cm)×71.84×10⁻⁴. If only RA area absolute or RA area indexed was given 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 cutoff values for normal RA areas for women and men, we used 95% quantiles and their 95% confidence intervals (CIs). The values were calculated with and without assuming a normal distribution using SAS version 9.2 (SAS Institute Inc, Cary, NC). The calculation assuming nonnormally distributed values led to nearly identical quantiles and CIs; therefore, we present the results assuming normality. The comparison of 95% quantiles between men and women and between groups with different exercise training status was performed with the SAS QUANTREG procedure.

Analysis of Determinants
We calculated correlation coefficients to describe determinants of RA area. Additionally, groups with different exercise training status was performed with the SAS QUANTREG procedure.
training status (ie, endurance-exercise training, strength-exercise training, or nonathletes) and sex groups were compared by ANOVA. Multivariate regression analysis was performed to take age, BSA, and sex into account simultaneously. Values of $P<0.05$ were considered statistically significant. For these analyses, we used IBM SPSS 20 (SPSS Statistics version 20, IBM Corp, Somers, NY).

**Literature Analysis**

Because only aggregated data, namely means, standard deviations, and sample sizes, are given in the literature, we estimated the 95% percentile assuming normally distributed data. Additionally, 95% CIs for the 95% percentile were determined by using the 97.5% CIs 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. From the pooled mean and the pooled standard deviation, the 95% percentiles and their 95% CIs were estimated as described above.

To analyze the influence of single studies on the pooled estimate, a sensitivity analysis was performed by leaving out 1 study at a time 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/Nonathletes**

We prospectively assessed 880 healthy adults: 230 nonathletes, 255 strength athletes, and 395 endurance athletes (Table 1 and Figures 2 and 3). Mean age was 28.2±10.5 years (range, 18–45 years) and did not differ significantly between groups. The mean absolute and indexed RA area values with standard deviations, the 95% quantiles, and the range of CIs are shown in Table 1. The 95% quantiles that have been defined as cutoff values for normal RA area were almost identical in nonathletes and strength athletes. In nonathletes, the 95% quantiles were significantly different between men and women ($P=0.0042$): 15.1 cm$^2$ (CI, 14.3–16.0) in women, 15.7 cm$^2$ (CI, 15.1–16.5) in men, and 15.5 cm$^2$ (CI, 15.1–15.9) in the mixed-sex group (Table 1). RA area indexed for BSA in nonathletes was 8.2 cm$^2$/m$^2$ in women, 8.4 cm$^2$/m$^2$ in men, and 8.3 cm$^2$/m$^2$ in the mixed-sex group (Table 1).

**Correlation Analysis of RA Area With Age, Sex, BSA, and Exercise Training Status**

RA area means were significantly different among nonathletes (12.5±2.0 cm$^2$), strength athletes (12.7±1.6 cm$^2$), and endurance athletes (15.4±2.1 cm$^2$; $P<0.0001$, ANOVA; Figure 2A) and

**Table 1. Characteristics of Pooled Analysis of Selected Studies on Right Atrial Area by 2-Dimensional Echocardiography**

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>n</th>
<th>Retrospective Study Design</th>
<th>Women, %</th>
<th>BSA</th>
<th>Sex Distinction</th>
<th>Area</th>
<th>Mean Age, y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ref. 22</td>
<td>1979</td>
<td>25</td>
<td>X</td>
<td>44</td>
<td></td>
<td></td>
<td>X</td>
<td>Men</td>
</tr>
<tr>
<td>Ref. 23</td>
<td>1983</td>
<td>11</td>
<td>X</td>
<td>27</td>
<td></td>
<td></td>
<td>X</td>
<td>Men</td>
</tr>
<tr>
<td>Ref. 19</td>
<td>1984</td>
<td>30</td>
<td>?</td>
<td>50</td>
<td>X</td>
<td></td>
<td>X</td>
<td>Men</td>
</tr>
<tr>
<td>Ref. 19</td>
<td>1984</td>
<td>67</td>
<td>?</td>
<td>50</td>
<td></td>
<td></td>
<td>X</td>
<td>Men</td>
</tr>
<tr>
<td>Ref. 20</td>
<td>1984</td>
<td>54</td>
<td>X</td>
<td>46.3</td>
<td></td>
<td></td>
<td>X</td>
<td>Men</td>
</tr>
<tr>
<td>Ref. 18</td>
<td>1986</td>
<td>43</td>
<td>?</td>
<td>51.2</td>
<td>X</td>
<td></td>
<td>X</td>
<td>Men</td>
</tr>
<tr>
<td>Ref. 21</td>
<td>2007</td>
<td>160</td>
<td>X</td>
<td>37.5</td>
<td>X</td>
<td></td>
<td>X</td>
<td>Men</td>
</tr>
<tr>
<td>Ref. 24</td>
<td>2009</td>
<td>15</td>
<td>?</td>
<td>53</td>
<td></td>
<td></td>
<td>X</td>
<td>Men</td>
</tr>
<tr>
<td>Ref. 25</td>
<td>2010</td>
<td>219</td>
<td>X</td>
<td>54.3</td>
<td></td>
<td></td>
<td>X</td>
<td>Men</td>
</tr>
<tr>
<td>Sum</td>
<td></td>
<td>624</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

Abs. indicates absolute; and BSA, body surface area.

Studies are listed in chronologic order of publication year.

**Figure 2.** Determinants of right atrial (RA) area. **A**, Type of training. **B**, Sex. **A**, Whisker plot illustrating the effect of endurance and strength training on RA area, prospectively evaluated. Endurance athletes had significantly larger RA areas compared with nonathletes and strength athletes. **B**, Significantly different RA area sizes in male and female nonathletes. The boxes represent the values of all subjects between the 25% and 75% quantiles (median line; the range from 5% to 95% quantiles is shown by the whiskers.
between men and women of the nonathletic group \((P=0.0042\); Figure 2B). If sex, age, BSA, and training status were taken into account simultaneously, only the correlations of RA area with endurance training and BSA, but not sex, 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 nonathletes and strength athletes \((n=485)\). In endurance athletes \((n=395)\), a weak correlation between RA area and age \((r=0.23, P<0.0001)\) and between RA area and BSA \((r=0.29, P<0.0001)\) occurred. Only 3% of the variability of RA area could be explained by age; 11% could be explained by BSA.

The different RA areas in men and women were confirmed in the pooled analysis of those previously published studies that distinguished between sexes. In all of these studies,\(^{18,19,21}\) we found significantly different mean RA areas in men and women, ranging from 2.6 to 3.0 cm\(^2\). 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 were given 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 databases and Cochrane databases for RA size. Two of the 11 studies were excluded.\(^{2,26}\) The second oldest of the 11 studies from Reeves et al\(^{26}\) identified a mean value of RA area of 16.1±3.4 cm\(^2\) in a mixed-sex cohort of 21 healthy control subjects. However, they used a sector-scan echocardiography Picker 80-C cardiac imager that was technically limited; echocardiographic 4-chamber views were different.\(^{26}\) The data of Raymond et al\(^{12}\) were not included because the RA area index was calculated from height instead of BSA. Therefore, because no mean height was provided, we were unable to calculate the absolute or indexed values for RA area.

Thus, 9 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 ECGs and physical examinations to exclude any heart disease. In 1 study, catheterization of the right and left sides of the heart had been performed.\(^{26}\) In addition, in this study, rubber casts fashioned from the right-side chambers during necropsy had been assessed in 8 deceased subjects without clinical or anatomic evidence of heart–lung diseases to validate the echocardiographic dimensions of the heart chambers.\(^{22}\) Overall, the assessed subjects were between 18 and 70 years; the mean age ranged between 22.2±4.5 years\(^{21}\) and 45 years\(^{22}\) (Table 2). Most subjects were <50 years of age. The sample size ranged from 11 to 219 subjects per study. The percentage of women ranged from 27% to 54.3%, although 1 study did not mention sex 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 4 studies\(^{21–25}\) used healthy subjects as the control group.

Table 3 summarizes the mean values for absolute and indexed RA area, standard deviations, 95% quantiles, and

<table>
<thead>
<tr>
<th>Table 2. Right Atrial Area Prospectively Obtained in 880 Healthy Subjects</th>
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<tbody>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>--------------------------------------------</td>
</tr>
<tr>
<td>No. (%)</td>
</tr>
<tr>
<td>Men</td>
</tr>
<tr>
<td>Women</td>
</tr>
<tr>
<td>RA area, cm(^2)</td>
</tr>
<tr>
<td>Men</td>
</tr>
<tr>
<td>Q-95 (CI)</td>
</tr>
<tr>
<td>Women</td>
</tr>
<tr>
<td>Q-95 (CI)</td>
</tr>
<tr>
<td>Mixed</td>
</tr>
<tr>
<td>RA area index, cm(^2)/m(^2)</td>
</tr>
<tr>
<td>Men</td>
</tr>
<tr>
<td>Q-95 (CI)</td>
</tr>
<tr>
<td>Women</td>
</tr>
<tr>
<td>Q-95 (CI)</td>
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<tr>
<td>Mixed</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; Q-95, 95% quantile; and RA, right atrial.
their 95% CIs 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 based on sex and training status are shown. The mean absolute RA area ranged from 4 cm² (which we considered implausible, so we excluded the values from further calculation) to 6.6 cm² in female nonathletes to 21.2 cm² in male endurance athletes. In each study, values for the 95% quantiles and CIs were calculated and compared with the values we obtained in our study population in 880 healthy subjects.

**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 378 men, 260 women, and 1012 unknown-sex nonathletes and strength athletes and 305 male and 170 female endurance athletes. We included nonathletes and strength athletes in the normal group because their RA distributions are very similar. The means were derived from values of the 9 studies of the pooled analysis and our own prospectively data of 880 healthy subjects. Figure 3 illustrates the 95% quantiles and CIs of RA area assigned to the analyzed studies and subgroups. Overall, in strength/nonstrength athletes, the pooled mean RA area was 12.2±1.8 cm² in women, 13.0±1.9 cm² in men, and 12.6±3.0 cm² in the mixed-sex group (Table 3). Pooled 95% quantiles of RA area were 15.2 cm² in women, 16.2 cm² in men, and 17.5 cm² in mixed-sex group (Table 3 and Figure 3). Pooled 95% quantiles of RA areas indexed for BSA were 8.5 cm²/m² (8.3–8.8 cm²/m²) in women, 8.6 cm²/m² (8.4–8.8 cm²/m²) in men, and 10.1 cm²/m² (9.9–10.4 cm²/m²) in the mixed-sex group.

**Sensitivity Analysis**

Without our prospectively obtained data, the reference values for the mixed-sex group were slightly higher, and without the values from Kelly et al., they were slightly lower (16.7 cm²). For women, no study had a remarkable influence. The leave-one-out estimates for the reference values for men varied between 15.9 and 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) between 18 and 70 years of age (most of them
<50 years of age) up to now. The calculated reference values for RA size obtained by 2-dimensional echocardiography in the apical 4-chamber view are based on almost all prospective and retrospective studies published so far. This is the first study to provide normal reference values for RA size. The study confirms that absolute cutoff values should be determined and used sex-specifically. Absolute cutoff values for RA area in nonathletes/strength athletes were significantly different in women (15 cm²) and men (16 cm²), whereas values indexed for BSA were similar in both sexes (women, 8.5 cm²/m²; men, 8.6 cm²/m²). Age, sex, BSA, and high-level endurance exercise training were identified as determinants of RA area. Top-level endurance athletes exceeded the reference values of RA area for nonathletes and strength athletes and showed no significant differences between men and women.

RA size evaluated by 2-dimensional echocardiography correlated well with rubber casts of heart chambers 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 function⁵,⁸ and is important for follow-up assessment and risk stratification in patients with right-sided heart failure such as patients with pulmonary hypertension.⁹,¹⁰ Furthermore, enlarged RA area belongs to the echocardiographic parameters that might raise or reinforce suspicion of pulmonary hypertension independently of tricuspid regurgitation velocity⁹,¹⁰ and may be an early indicator for primary diseases of the right side of the heart. RA area distinguished healthy subjects from patients with RV volume overload or rightsided heart diseases with only minimal overlap between the groups,²,²²,²³,²⁵ as long as correct cutoff values were used.

Furthermore, an enlarged atrium may be an early indicator of pulmonary hypertension and primary diseases of the right side of the heart.

For clinical practice, it is more convenient to measure the absolute area instead of performing the corrections for BSA. Therefore, the finding that women and men have significantly different absolute RA areas is of clinical importance and has already been observed in small cohorts of healthy subjects.¹⁸–²⁰ Nevertheless, sex differences in RA size have not been analyzed systematically so far and have not led to different sex-specific reference values.¹¹ This study confirms for the first time sex differences and the influence of age, BSA, and training status on echocardiographic RA area in a large number of healthy adult subjects. Mixed-sex values for absolute RA area¹¹ should therefore not be used any longer to avoid the risk of underestimation of RA enlargement, especially in women.

However, no significant sex differences were observed when RA area was corrected for BSA and training status (endurance athletes). Different reference values for men and women have also been documented for echocardiographic RV end-diastolic area.²⁸ Absolute RA area was significantly, but weakly, correlated with age. Older subjects had slightly enlarged RA areas. However, most subjects of this study were <50 years of age. In this cohort, age accounted for only 3% of the 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 women and 16 cm² for men to age. Nevertheless, further evaluation of children and healthy subjects >50 years of age is necessary to determine normal RA area in these groups.

Numerous studies have described “athlete’s heart syndrome” with chamber enlargement of the left and right sides of the heart.²⁹ However, the effect on RA size is less well evaluated. Acute, transient RA and RV dilatation, reduction of
endurance training were determinants of RA area. Further studies in children and subjects >50 years of age are needed.

Disclosures

None.

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Right atrial size is important in several indications such as screening, diagnosis, and follow-up assessment of patients with pulmonary hypertension. This is the first study to provide normal reference values for right atrial area in a large number of healthy subjects. Sex differences and the influence of age, body surface area, and training status on echocardiographic right atrial area are confirmed for the first time. Because an enlarged atrium may be an early indicator for pulmonary hypertension or primary diseases of the right heart, the results are of high clinical impact. For clinical practice, it is more convenient to measure the absolute area instead of performing corrections for body surface area. Therefore, the finding that women and men have significantly different absolute right atrial areas is of clinical importance. Cutoff values for right atrial area were significantly different in women (15 cm²) and men (16 cm²); therefore, sex-specific values should be used in the future.
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