Premature Atrial Contractions in the General Population
Frequency and Risk Factors

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Background—Premature atrial contractions (PACs) are independent predictors of atrial fibrillation, stroke, and death. However, little is known about PAC frequency in the general population and its association with other cardiovascular risk factors.

Methods and Results—We performed a cross-sectional analysis among participants of the population-based Swiss cohort Study on Air Pollution and Lung Diseases in Adults (SAPALDIA). 24-hour Holter electrocardiograms to assess PAC prevalence and frequency were performed in a random sample of 1742 participants aged ≥50 years. The median (interquartile range) number of PACs per hour was 0.8 (0.4–1.8), 1.1 (0.5–2.4), 1.4 (0.7–4.6), 2.3 (0.8–6.9), and 2.6 (1.2–6.5) among participants aged 50 to 55, 55 to 60, 60 to 65, 65 to 70, and ≥70 years, respectively (P<0.0001). Only 18 (1.0%) participants did not have at least 1 PAC during Holter monitoring. In multivariable negative binomial regression models, PAC frequency was significantly associated with age (risk ratio [RR] per SD 1.80; P<0.0001), height (RR per SD 1.52; P<0.0001), prevalent cardiovascular disease (RR 2.40; P<0.0001), log-transformed N-terminal pro B-type natriuretic peptides (RR per SD 1.27; P<0.0001), physical activity ≥2 hours per day (RR 0.69; P=0.002), and high-density lipoprotein cholesterol (RR per SD 0.80; P=0.0002). Hypertension and body mass index were not significantly related to PAC frequency.

Conclusions—To our knowledge, this is the first study to assess risk factors for PAC frequency in the general population aged ≥50 years. PACs are common, and their frequency is independently associated with age, height, history of cardiovascular disease, natriuretic peptide levels, physical activity, and high-density lipoprotein cholesterol. The underlying mechanisms of these relationships need to be addressed in future studies. (Circulation. 2012;126:2302-2308.)

Key Words: atrial fibrillation ■ atrial premature complexes ■ cardiovascular diseases ■ epidemiology ■ risk factors

Atrial fibrillation (AF) is a highly prevalent arrhythmia associated with an increased risk of death, stroke, and congestive heart failure.2,3 In recent years, multiple risk factors for AF occurrence have been described, including age, elevated blood pressure, body size, and inflammation.1,4–8 Most of these risk factors, in particular age, hypertension, and body size, are important determinants of left atrial (LA) enlargement,9,10 suggesting that LA structural remodeling is an important mediator for AF occurrence.11,12

Clinical Perspective on p 2308

Similar to the effect of LA structural remodeling, an increased number of premature atrial contractions (PACs) and subclinical atrial tachyarrhythmias have been shown to be strong and independent predictors of incident AF and associated complications,13–18 pointing to an important role of atrial electric activity in AF initiation and maintenance.19–21 However, and in contrast to the structural LA component, few if any population-based studies have
assessed risk factors for an increased atrial electric activity in general and PAC frequency in particular.

Therefore, the aim of the present study was to assess the prevalence of and risk factors for PAC frequency in a large representative sample of the general population aged ≥50 years.

**Methods**

**Participants**

Design and objectives of the Swiss Cohort Study on Air Pollution and Lung Diseases in Adults (SAPALDIA) have been described previously. In brief, 9651 randomly selected adults, aged 18 to 60 years, from 8 different areas of Switzerland that were chosen to represent the variety of environmental conditions in respect to geography, climate, degree of urbanization, and air pollution in Switzerland had a baseline health interview and health examinations in 1991. During a follow-up visit in 2002, 8047 of the original participants were reassessed. Every effort was taken to track enrolled participants for the 2002 follow-up visit, and only 6.8% of the 9651 original participants were lost to follow-up, as previously described. A random subsample of all 4417 participants aged ≥50 years were invited to undergo 24-hour Holter monitoring, and 1846 subjects (955 women, 891 men) agreed to participate. Using inverse probability weighting, we only observed minimal changes in effect estimates, suggesting that potential bias resulting from differential noninclusion or nonparticipation in the 24-hour Holter monitoring study would be small (data not shown).

Exclusion criteria for the Holter monitoring were general or spinal anesthesia within 8 days before the recording (n=5), a myocardial infarction within 3 months (n=2), and taking digitalis (n=6). None of the participants had a previous pacemaker implantation. After exclusion of recordings showing AF (n=12), recordings of <18 hours duration (n=73), and recordings of insufficient quality (n=6), 1742 (94.4%) subjects with valid Holter recordings were retained for this analysis. The protocol was approved by all regional ethics committees, and all participants gave written informed consent.

**Study Variables**

For the current analysis, all covariate information and Holter data were obtained at the 2002 SAPALDIA follow-up visit. During the 2002 health interview, standardized information was obtained on age, history of hypertension, diabetes mellitus, smoking, alcohol consumption, physical exercise, highest education level achieved (primary school, secondary school, or college/university degree), a previous history of cardiovascular disease, and intake of β-blockers or calcium channel blockers. Height, weight, and blood pressure (mean of 2 measurements performed according to the World Health Organization recommendations) were directly measured in a standardized manner. For the current analysis, hypertension was defined as a history of hypertension, a mean visit systolic blood pressure ≥140 mm Hg, or a mean visit diastolic blood pressure ≥90 mm Hg. Prevalent cardiovascular disease was defined as having physician confirmed heart disease reported on the questionnaire.

**Laboratory Measurements**

Biomarkers used for the current study were assayed from nonfasting frozen serum samples by the Institute for Clinical Chemistry at the University Hospital Zürich, Switzerland. Lipids were determined according to standard methods; low-density lipoprotein cholesterol was calculated using the Friedewald formula for subjects who had fasted for ≥6 hours and had triglyceride levels of ≤4.7 mmol/L. High-sensitivity troponin T and N-terminal pro B-type natriuretic peptides (NT-proBNP) were quantified using the Elesys E170 electrochemoluminescence immunoassay analyzer from Roche diagnostics. According to the package insert of the manufacturer, a NT-proBNP value ≥125 ng/L was considered elevated. The 10% functional assay sensitivity and the limit of quantification of the troponin T test are 13 and 3 ng/L, respectively. The interassay imprecision of NT-proBNP was 3%.

**Holter Recording**

Holter recordings were performed between August 2001 and March 2003. Participants were asked to follow their regular daily routine and to complete a time-activity diary during the recording period. We used digital devices (Aria, Del Mar Medical Systems, Irvine, CA) with a frequency response of 0.05 to 40 Hz and a resolution of 128 samples/s for 24-hour Holter recording. Three lead monitoring (V1, altered V3 with the electrode on the left midclavicular line on the lowest rib and altered V5 with the electrode on the left anterior axillary line on the lowest rib) was obtained, and mean (SD) duration of the recording period was 22.3 (2.1) hours.

All recordings were scanned through a StrataScan 563 (Del Mar) and interpreted using the interactive method. The system was programmed to stop at all rhythmic event or ectopic beat, corresponding to a true count of all events on the full disclosure. A PAC was defined by a coupling interval to the preceding QRS complex <80% of the mean RR interval before the event, and a QRS duration of <0.12 seconds unless aberration was suspected. The total number of PACs was summed during the entire recording period. To account for the slight variations in recording time, the mean number of PACs per hour was used as the primary outcome variable in this study. The definition of heart rate variability (HRV) measures has been described in detail previously. Total power spectral density (TP) was defined as frequency domain ≤0.40 Hz.

**Statistical Analysis**

Baseline characteristics below and above the median PAC count per hour were compared using Wilcoxon rank sum tests or Kruskal-Wallis tests for continuous variables and χ² tests for categorical variables. The distribution of continuous variables was assessed using skewness, kurtosis, and visual inspection of the histogram.

Multivariable negative binomial regression analysis was performed to identify independent correlates for the number of PACs per hour. Variables entered into the model were age, sex, body mass index (calculated as weight in kg/height in m squared), hypertension, history of cardiovascular disease, smoking, alcohol consumption, physical activity, current use of calcium channel blockers or β-blockers, high-density lipoprotein (HDL) cholesterol, troponin T, and NT-proBNP. Covariates with a skewed distribution were log-transformed to improve the linearity of the association. Coefficients of continuous variables were estimated for a 1 SD change, to improve comparability across variables.

To assess whether other Holter measures such as the number of premature ventricular contractions (PVCs) or HRV measures were associated with PAC frequency, we alternatively added the number of PVCs and TP to 2 separate multivariable models. Spearman correlation coefficients were used to assess univariate relationships between PAC frequency, PVC frequency, and TP.

Subgroup effects for age, sex, current smoking, and prevalent cardiovascular disease were tested using multiplicative interaction terms in the multivariable regression models. Categorical variables were entered in the regression models using binary indicator variables. All analyses were performed using SAS version 9.2 (SAS Institute Inc, Cary, NC). A 2-tailed P value <0.05 was prespecified to indicate statistical significance.

**Results**

Baseline characteristics stratified by the median number of PACs per hour are shown in Table 1. Compared with individuals with <1.27 PACs per hour, those with ≥1.27 PACs per hour were significantly older (P<0.0001), had a higher systolic blood pressure (P=0.004), a higher prevalence of cardiovascular diseases (P=0.003), a lower education level (P=0.04), a higher HDL cholesterol (P=0.02), and higher levels of NT-proBNP and troponin T (both P<0.0001). Individuals with a higher
Table 1. Baseline Characteristics Stratified by the Median No. of PACs per Hour

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>&lt;1.27 PACs/h (n=869)</th>
<th>≥1.27 PACs/h (n=873)</th>
<th>P</th>
<th>Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of PACs per hour</td>
<td>0.6 (0.3–0.9)</td>
<td>3.7 (2.0–9.6)</td>
<td>.</td>
<td>...</td>
</tr>
<tr>
<td>Male, %</td>
<td>434 (49.9)</td>
<td>413 (47.3)</td>
<td>0.27</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>58 (54–63)</td>
<td>63 (57–67)</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Height, m</td>
<td>1.68 (1.61–1.74)</td>
<td>1.67 (1.61–1.75)</td>
<td>0.48</td>
<td></td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>26.3 (23.7–29.0)</td>
<td>26.3 (23.7–29.3)</td>
<td>0.95</td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>131 (118–142)</td>
<td>132 (121–146)</td>
<td>0.004</td>
<td></td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>82 (75–88)</td>
<td>82 (75–89)</td>
<td>0.76</td>
<td></td>
</tr>
<tr>
<td>History of hypertension, %</td>
<td>386 (44.4)</td>
<td>416 (47.7)</td>
<td>0.18</td>
<td></td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>6.2 (5.5–7.1)</td>
<td>6.2 (5.6–6.9)</td>
<td>0.67</td>
<td></td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.4 (1.2–1.7)</td>
<td>1.5 (1.2–1.8)</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>1.7 (1.2–2.6)</td>
<td>1.6 (1.1–2.4)</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>78 (9.0)</td>
<td>93 (10.7)</td>
<td>0.24</td>
<td></td>
</tr>
<tr>
<td>Current smoking, %</td>
<td>183 (21.1)</td>
<td>154 (17.7)</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>History of cardiovascular disease, %</td>
<td>50 (5.8)</td>
<td>83 (9.5)</td>
<td>0.003</td>
<td></td>
</tr>
<tr>
<td>Intake of β-blockers, %</td>
<td>80 (9.2)</td>
<td>102 (11.7)</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>Intake of calcium channel blockers, %</td>
<td>35 (4.0)</td>
<td>46 (5.3)</td>
<td>0.22</td>
<td></td>
</tr>
<tr>
<td>Alcohol consumption, %</td>
<td></td>
<td></td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>&lt;1×/day</td>
<td>589 (68.1)</td>
<td>590 (68.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;1–2×/day</td>
<td>177 (20.5)</td>
<td>153 (17.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥3×/day</td>
<td>99 (11.5)</td>
<td>125 (14.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Highest education level, %</td>
<td></td>
<td></td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Primary school</td>
<td>63 (7.3)</td>
<td>90 (10.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary school</td>
<td>572 (65.8)</td>
<td>574 (65.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>College or university degree</td>
<td>234 (26.9)</td>
<td>208 (23.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical activity, %</td>
<td></td>
<td></td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>Rarely/never</td>
<td>347 (40.4)</td>
<td>374 (43.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.5 to 1 h/day</td>
<td>275 (32.1)</td>
<td>292 (33.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥2 h/day</td>
<td>236 (27.5)</td>
<td>198 (22.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NT-proBNP, ng/L</td>
<td>47 (28–82)</td>
<td>78 (45–135)</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>NT-proBNP ≥125 ng/L</td>
<td>82 (11.7)</td>
<td>182 (26.5)</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Troponin T levels, µg/L</td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>&lt;0.003</td>
<td>287 (40.9)</td>
<td>261 (38.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.003–0.014</td>
<td>405 (57.8)</td>
<td>387 (56.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥0.014</td>
<td>9 (1.3)</td>
<td>38 (5.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of PVCs per hour</td>
<td>0.1 (0.0)</td>
<td>0.6 (0.1, 6.2)</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Total power, ms²</td>
<td>3518 (2304, 5243)</td>
<td>4017 (2580, 5806)</td>
<td>0.0002</td>
<td></td>
</tr>
</tbody>
</table>

Data are median (interquartile range) or numbers (percentages). No. of observations across categories may not sum to the given No. because of missing data.

PAC indicates premature atrial contraction; HDL, high-density lipoprotein; NT-proBNP, N-terminal pro-B-type natriuretic peptide; and PVC, premature ventricular contraction.

*Based on Wilcoxon rank sum tests for continuous variables and χ² tests for categorical variables.

Figure 1. Number of PACs per hour stratified by 5-year age categories. Data are medians, whiskers represent interquartile ranges. The P value is based on a Kruskal-Wallis test across age categories. PAC indicates premature atrial contraction.

PAC frequency also had a higher number of PVCs and a greater HRV (P<0.0001 and P=0.0002, respectively). There was no significant difference in sex, hypertension prevalence, body mass index, intake of β-blockers, and intake of calcium channel blockers (Table 1). Because sex was not associated with the number of PACs, all analyses were performed in the overall sample.

PACs were highly prevalent in the current study population. Only 18 of 1742 (1.0%) participants did not have at least 1 PAC on 24-hour Holter monitoring. As shown in Figure 1, the median number (interquartile range) of PACs per hour was 0.8 (0.4–1.8), 1.1 (0.5–2.4), 1.4 (0.7–4.6), 2.3 (0.8–6.9), and 2.6 (1.2–6.5) among participants aged 50 to 55, 55 to 60, 60 to 65, 65 to 70, and ≥70 years, respectively (P<0.0001).

At least 70 PACs during Holter monitoring were observed in 478 (27.4%) participants. Again, the prevalence increased across the age strata 50 to 55 (14.0%), 55 to 60 (20.1%), 60 to 65 (31.4%), 65 to 70 (42.4%), and ≥70 years (46.7%) (P<0.0001), as shown in Figure 2.

Results from the multivariable regression models are shown in Table 2. Independent correlates for the number of PACs per hour were age (Risk ratio [RR] per SD 1.80; P<0.0001), height (RR per SD 1.52; P<0.0001), a history of cardiovascular disease (RR 2.40; P<0.0001), log-transformed NT-proBNP (RR per SD 1.27; P<0.0001), HDL cholesterol (RR per SD 0.80; P=0.0002), and at least 2 hours of physical exercise per day (RR 0.69; P=0.002). The nonsignificant relationship of height with the number of PACs per hour in univariate analysis (Table 1) was mainly explained by the confounding influence of age and sex (RR per SD 1.47, P<0.0001 after adjustment for age and sex).

The number of PVCs was moderately correlated with PAC frequency (r=0.32, P<0.0001). In a multivariable model, the number of PVCs per hour (log transformed) was significantly associated with PAC frequency (RR, 1.17; 95% confidence interval, 1.14–1.21, P<0.0001). TP was weakly correlated with PAC frequency (r=0.11; P<0.0001). After multivariable adjustment, TP remained significantly associated with
PAC frequency (RR, 1.45; 95% confidence interval, 1.24–1.71; \( P<0.0001 \)).

In subgroup analyses, we found no evidence that the effect of age, height, NT-proBNP, exercise, and HDL cholesterol differed by sex, smoking status, and age (all \( P \) values for interaction >0.05). However, the effect of cardiovascular disease was much stronger among women than among men (RR 5.30 versus 0.90; \( P \) for interaction <0.0001). We also found a significant interaction of age (\( P \) for interaction 0.002), height (\( P \) for interaction 0.002), and HDL cholesterol (\( P \) for interaction 0.0002) with prevalent cardiovascular disease, suggesting that the association between these factors and PAC frequency significantly differed among participants with compared with those without cardiovascular disease, as shown in Table 3.

### Discussion

In this large population-based study of individuals aged \( \geq 50 \) years, we found that 99% of all participants did have at least 1 PAC during 24-hour Holter monitoring. The PAC prevalence strongly increased with age from a median of 0.8 per hour among participants aged 50 to 55 years to 2.6 per hour among those aged \( \geq 70 \) years. These data are consistent with a smaller study among elderly individuals from the Cardiovascular Health Study.25 To our knowledge, this is one of the first studies to assess risk factors associated with PAC frequency in the general population. Our data show that age, height, history of cardiovascular disease, physical activity, natriuretic peptide levels, and HDL cholesterol were significantly associated with the number of PACs. Although independent replication of our findings in other samples is needed, we nevertheless believe that this study improves our knowledge on this common phenomenon.

The importance of PACs in the initiation and maintenance of AF has been suggested in several studies.13–16,26,27 For example, PACs have previously been associated with an increased risk of incident AF in population based cohort studies.13–16 Furthermore, Inoue et al found that ablation of PACs in addition to pulmonary vein isolation was associated with a high probability of recurrence-free survival among patients with persistent AF undergoing catheter ablation, suggesting that these electric triggers may play an important role in AF initiation.28 In addition, subclinical atrial arrhythmias like PACs or pacemaker-detected atrial tachyarrhythmias have been related to an increased risk of stroke and death.13–18 Taken together, although our study may not have immediate clinical implications, more data are urgently needed to better understand the significance of our findings that PACs are present in the great majority of individuals aged \( \geq 50 \) years.

A history of cardiovascular disease and levels of natriuretic peptides were strongly related with PAC frequency in this study, and the association with elevated troponin levels was of borderline significance. The relatively small number of individuals with elevated troponin levels may have limited our power to show an association. As shown in many previous studies, elevated levels of natriuretic peptides and troponin probably reflect a higher burden of subclinical and clinical structural heart disease and increased wall stress,28–31 which in turn may favor PAC occurrence.15 The fact that PVC

### Table 2. Multivariable Negative Binomial Regression Model to Assess Correlates for the No. of PACs per Hour

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Risk Ratio*</th>
<th>95% Confidence Interval</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, per SD</td>
<td>1.80</td>
<td>1.60–2.02</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sex</td>
<td>1.37</td>
<td>0.98–1.91</td>
<td>0.07</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.95</td>
<td>0.76–1.18</td>
<td>0.61</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>2.40</td>
<td>1.64–3.51</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Body mass index, per SD</td>
<td>0.97</td>
<td>0.87–1.07</td>
<td>0.55</td>
</tr>
<tr>
<td>Current smoking</td>
<td>1.27</td>
<td>0.99–1.63</td>
<td>0.06</td>
</tr>
<tr>
<td>Height, per SD</td>
<td>1.52</td>
<td>1.30–1.78</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Log NT-proBNP, per SD</td>
<td>1.27</td>
<td>1.13–1.42</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

**Troponin levels**

- <0.003: Reference
- 0.003–0.014: 1.09, 0.99–1.20, 0.08
- \( \geq 0.014 \): 1.18, 0.99–1.40, 0.07

**HDL cholesterol, per SD**

- 0.80: 0.71–0.90, 0.0002

**Physical activity**

- Rarely/never: Reference
- 0.5–1 h/day: 0.92, 0.74–1.15, 0.46
- \( \geq 2 \) h/day: 0.69, 0.54–0.87, 0.002

**Calcium channel blockers**

- 0.99: 0.63–1.56, 0.97

**\( \beta \)-blockers**

- 0.78: 0.55–1.11, 0.17

**Alcohol consumption**

- <1× per day: Reference
- 1–2× per day: 0.96, 0.75–1.23, 0.74
- \( \geq 3 \)× per day: 0.84, 0.62–1.13, 0.25

HDL indicates high-density lipoprotein; NT-proBNP, N-terminal pro-B-type natriuretic peptide; and SD, standard deviation.

*Data are risk ratios per 1 SD increase for continuous variables or compared with the reference category for categorical variables. Risk estimates for all covariates are adjusted for age, sex, body mass index, hypertension, cardiovascular disease, smoking, height, physical activity, alcohol consumption, use of calcium channel blockers or \( \beta \)-blockers, HDL-cholesterol, NT-proBNP, and troponin.

![Figure 2. Proportion of individuals with >70 PACs during the recording period. Data are percentages. The \( P \) value is based on a \( \chi^2 \) test across age categories. PAC indicates premature atrial contraction.](http://circ.ahajournals.org/figure.html)
frequency was strongly associated with PAC frequency may suggest that mechanisms for the occurrence of atrial and ventricular premature contractions partly overlap. The positive association between HRV and PAC frequency could be attributable in part to failure to exclude PACs from the RR intervals in the HRV analysis. Future studies using echocardiography or other imaging tools are needed to clarify the mechanisms of how these cardiac biomarkers relate to an increased PAC burden in the community and whether the severity of the underlying cardiovascular disease may have an impact.

By contrast, it is relatively unclear how adult height is related to PAC burden and incident AF.8 It has been hypothesized that the increased risk among taller individuals is mainly a result of the close relationship between body size and LA size.8 Interestingly, we have previously shown that the significant relationship between birth weight and AF is completely attenuated after taking into account adult height,32 suggesting that genetic or early life determinants may play an important role. Taken together, the available evidence raises the intriguing possibility that the relationship between height and AF may be partly related to an elevated electric activity among taller individuals. Future studies are needed to further assess this hypothesis.

With regard to HDL-cholesterol, the strong inverse relationship with PAC frequency is in agreement with the overall inverse relationship between HDL cholesterol and cardiovascular disease.33 With regard to AF, the data are less clear. While 1 previous study found an inverse relationship between HDL cholesterol and incident AF among Japanese individuals,34 this finding could not be confirmed in a more recent analysis, where no significant association between HDL cholesterol and incident AF was observed after multivariable adjustment.35 In the same study, low-density lipoprotein cholesterol was inversely related to incident AF after extensive multivariable adjustment.35 Although the underlying mechanisms for these differing relationships are unclear, it has been shown that blood lipids could affect the composition of the cell membranes, a major determinant of cell excitability.36 In the future, the role of lipids and lipoproteins in arrhythmia development needs to be better defined.

We found an inverse relationship between physical activity and PAC frequency. These data are in agreement with at least 1 previous study that found an inverse relationship between the amount of moderate exercise and incident AF among elderly individuals.37 However, the association between exercise and AF occurrence is more complicated, as vigorous exercise has been related to an increased risk of AF.38

The fact that obesity and hypertension were not significantly related to PAC frequency also deserves comment. Many studies have shown that obesity and hypertension are the 2 most important potentially modifiable risk factors for incident AF39–41 and that they are strongly related to an elevated LA size.9,10 These data, in conjunction with the present findings, may suggest that obesity and hypertension are major determinants of structural LA remodeling but do not influence the electric activity of the atria.

**Strengths and Limitations**

Strengths of the present study include its population-based design, the large sample size, and the large number of 24-hour Holter recordings available for analysis. Several potential limitations also need to be taken into account for a balanced interpretation of this study. First, in this study we evaluated a white, middle-aged to elderly population-based sample, and our findings may not be generalizable to other populations or patient groups. Furthermore, the small number of individuals unwilling to participate or lost to follow-up22 may be different from those who finally participated in this study. Second, this was a cross-sectional analysis, precluding the possibility to infer causal relationships or provide clinical outcome data. Third, echocardiography was not available in our study, and future studies are needed to directly relate the current findings to structural cardiac alterations. Finally, the number of PACs recorded may have a certain day-to-day variability, which we were unable to assess, given that only 1 recording per individual was obtained. Assuming that this variability is random, this might have slightly reduced our power to detect significant associations.

**Conclusions**

In this large population-based study of individuals aged ≥50 years, only a small minority of participants did not have at least 1 PAC on 24-hour Holter monitoring. Risk factors for PAC frequency included age, height, a history of cardiovascular disease, physical activity, natriuretic peptide levels, and HDL cholesterol, but not hypertension and body mass index. These findings may suggest differential risk factors for structural and electric remodeling in the pathogenesis of AF. Given the high PAC prevalence in this population and its
negative prognostic impact, more studies are urgently needed to better understand this phenomenon.

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Disclosures
None.

References


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**CLINICAL PERSPECTIVE**

Although premature atrial contractions (PACs) have been associated with an increased risk of death, stroke, and atrial fibrillation, they are usually considered a benign phenomenon. Accordingly, little is known about the prevalence of and risk factors for PAC occurrence in the general population. In this study of individuals aged ≥50 years, we found that only 18 (1.0%) participants did not have at least 1 PAC during Holter monitoring. The number of PACs was strongly increasing with increasing age. In multivariable regression models, PAC occurrence was significantly associated with age, height, cardiovascular disease, exercise, and plasma levels of N-terminal pro B-type natriuretic peptides and high-density lipoprotein cholesterol. The underlying mechanisms of these relationships are currently unknown. Although obesity and hypertension are 2 of the most important risk factors for the occurrence of atrial fibrillation, they were not significantly associated with PAC burden in this study. These data could suggest that obesity and hypertension are major determinants of structural left atrial remodeling but do not influence the electric activity of the atria. Given the high prevalence of PACs in the population and its negative prognostic impact, more studies are needed to better understand this phenomenon.
Premature Atrial Contractions in the General Population: Frequency and Risk Factors
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