Familial Atrial Fibrillation Predicts Increased Risk of Mortality
A Study in Danish Twins

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Background—Atrial fibrillation (AF) is a common arrhythmia. Several studies have shown association of genetic variants with AF and that familial AF increases the risk of AF. We have previously shown a substantial heritability of AF in a twin study. The objective of this study was to determine whether having a co-twin with AF influences mortality.

Methods and Results—We identified all Danish twins with AF born during and after 1912 in the Danish Twin Registry, the National Patient Registry, and the Central Office of Civil Registration. For each twin, we randomly identified 4 twins without AF, matched on sex, zygosity, and age. We compared survival among the co-twins of the affected twins (co-cases, n=2164) and the co-twins of the unaffected twins (co-controls, n=8626). The co-cases showed increased death rates compared with the co-controls (hazard ratio, 1.20; 95% confidence interval, 1.11–1.30; P<0.0001), and this effect was more pronounced in monozygotic twins (hazard ratio, 1.30; 95% confidence interval, 1.09–1.55; P=0.003), compared with dizygotic same sex (hazard ratio, 1.16; 95% confidence interval, 1.04–1.29; P=0.006) and opposite sex twins (hazard ratio, 1.20; 95% confidence interval, 0.97–1.47; P=0.093).

Conclusions—The mortality rate was 20% higher in twins who had a co-twin with AF than in twins without familial AF. This effect was almost doubled in monozygotic twins compared with dizygotic twins, suggesting the influence of genetic factors. (Circ Arrhythm Electrophysiol. 2013;6:10-15.)

Key Words: atrial fibrillation ■ epidemiology ■ genetics ■ mortality ■ twin study

Atrial fibrillation (AF) is the most common cardiac arrhythmia, currently affecting ≈2.6 million Americans and 6 million Europeans, and the prevalence is increasing.1 The disease is associated with thromboembolic complications, chronic heart failure, and increased mortality.2 Much is known about the mechanisms of AF initiation and maintenance, but the molecular basis of the disease remains mostly unknown. Advancing age, male sex, obesity, hypertension, ischemic and valvular heart disease, myocardial infarction, and hyperthyroidism are the dominating risk factors for AF;3 although in 2% to 30% of the patients AF develops without any predisposing disease and at an early age, a condition classified as lone AF.4

Clinical Perspective on p 15

The Framingham Heart Study was the first large-scale, prospective population study to determine the impact of AF on risk of death. The study found that AF was associated with a 50% increase in risk of death for men and a 90% increase in women, when adjusting for clinical risk factors.3 In 2004, it was reported that parental AF was a risk factor for AF in offspring, increasing the risk 3-fold if any parent was affected and 6-fold if the mother was affected.6 A study on the Icelandic population has shown an increase in the relative risk of AF in individuals with an affected first-degree relative,7 and it was recently reported that familial AF is a risk factor for new-onset AF.8,9 Our research group has previously shown a substantial heritability of AF in Danish twins.10 The molecular basis of this familial aggregation of AF has been investigated in numerous studies, and variations in genes encoding ion channels and other proteins involved in cardiac electric activity have been identified.11,12 Some variations are rare mutations that cause disease in large families with clustering of AF, whereas others are common polymorphisms also found in patients with sporadic AF. Genetic variants associated with Brugada and long-QT syndrome have recently been found in patients with onset of lone before the age of 40, and 2 studies have identified pedigrees with overlapping phenotypes of lone AF and QTc-prolongation,13,14 indicating a substantial overlap between lone AF and diseases associated with increased risk of sudden cardiac death.15-17 These findings suggest that there is a genetic component in AF and that this arrhythmia represents a complex trait with multiple

Received February 27, 2012; accepted November 21, 2012.

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Circ Arrhythm Electrophysiol is available at http://circcep.ahajournals.org DOI: 10.1161/CIRCEP.112.971580
environmental and genetic contributing factors. Despite the great effort made in unraveling the pathogenesis of AF, we still know little about disease development, and the treatment available is not adequate. We know that first-degree relatives of patients with AF have increased risk of AF, and the recent associations between an AF phenotype and risk of sudden cardiac death raised the question whether these individuals also have increased mortality. We studied the survival patterns of Danish twins with and without AF, by combining data from 3 nationwide registries in Denmark.

Methods

The Central Office of Civil Registration

Since 1968, all Danish citizens have been registered in the Central Office of Civil Registration (the CPR registry) with a personal 10-digit civil registration number (CPR number) assigned at birth. The CPR registry was established for administrative purposes and contains updated information regarding name, sex, date of birth, citizenship, identity of parents, vital status, place of residence, and spouses. The quality of the information has not been validated, but it is generally accepted that it holds very high quality. Several factors support this: (1) registration is required by law, (2) the data are used continuously for administrative purposes, which corrects errors when they are encountered, and (3) there is ongoing validation of the information recorded.

The Danish Twin Registry

The Danish Twin Registry (DTR) is a nationwide, population-based registry established in 1954. It holds information on >80,000 twin pairs born between 1870 and 2010 identified through church records or through the CPR registry. All twins are ascertainment independent of disease. Zygosity is self-reported and established through a questionnaire with questions on the degree of similarity between twins in a pair. This classification has been evaluated through blood samples, and misclassification has been found to be <5%. The ascertainment of twins in the registry was conducted using 4 different methods, depending on the birth cohorts, mainly because the CPR registry was first available from its founding in 1968. This led to distinct follow-up in 3 groups of birth cohorts: twins born during 1870–1930 were included in the DTR if they survived until age 6, twins born during 1931–1968 were included if they were alive on April 1, 1968, and twins born after 1968 were included at birth. In the birth cohorts 1911–1930, only same-sexed twin pairs were reported. The estimated coverage in 1870–1968 is almost 90%, whereas ascertainment is complete from 1968 to 2010.

The Danish National Patient Registry

When a patient visits an emergency room, a outpatient department, or is admitted to a hospital in Denmark, diagnoses according to the International Classification of Disease is registered in the Danish National Patient Registry (NPR). The NPR includes information on >80

Population

The CPR number was used to link information from the CPR registry, the DTR, and the NPR. We identified 2505 twins who were diagnosed with AF in the period 1977–2010. Of these, 2143 twin pairs were discordant for AF, meaning that only 1 twin in each pair had AF, and 181 pairs were concordant, meaning that both twins had AF. In discordant pairs, the twin diagnosed with AF was defined as the index twin, whereas in concordant pairs, the twin diagnosed first was defined as the index twin. All twins born before January 1, 1912, were excluded to ensure that no twin was >65 years at onset of registration of the AF diagnosis in the NPR. This lead to a total of 2164 index twins: 440 monozygotic (MZ), 1591 dizygotic (DZ), and 133 with unknown zygosity. For each of these, we randomly selected 4 controls matched regarding sex and zygosity, from twins who were alive and without AF at the time of diagnosis of the affected twin. In addition, the controls had to be alive and not diagnosed with AF at the age where the index twin was diagnosed with AF. In cases where <4 twins fulfilled the matching criteria (n=12), we included all available controls. To estimate the effect of having a co-twin with AF on mortality, we included the co-twins of the index twins, entitled co-cases (n=2164), and the co-twins of the controls, entitled co-controls (n=8626) and compared their survival. This design enabled determination of the survival patterns from the time the twins entered the DTR and not only from the time of diagnosis of the affected twin. A similar method has been used in a study on twins with implanted pacemakers. The prevalence of structural heart disease, hypertension, pulmonary and endocrine disorders registered in the NPR was assessed for each group. To examine possible confounding effects of cardiopulmonary diseases that are known to increase risk of both AF and death, we performed the same survival analysis as described above in 2 additional subsets. First, we included only co-twins of index twins with lone AF and controls that did not have any of these diagnoses at the time of diagnosis of the index twin. Co-twins of index twins with a diagnosis of cardiopulmonary disease, thyreotoxicosis, or diabetes mellitus before or within 2 years of their AF diagnosis were excluded. The diagnoses used in identifying these twins can be seen in Table 1. Second, we excluded all co-cases and co-controls with a co-twin diagnosed with heart failure or cardiomyopathy and included the remaining twins in a stratified Cox regression model.

Statistical Analysis

The co-cases and the co-controls were followed from entry in the DTR until death, emigration or end of follow-up, whichever came first. Follow-up ended at January 1, 2011. The survival in the 2 groups was compared using a stratified Cox regression model to allow for matching design. Thus, we fitted a Cox regression model with the only covariate being co-case or co-control identity, but where the baseline function was allowed to vary across matching group. To explore whether differences between the co-cases and the co-controls were dependent on zygosity and sex, we then performed a stratified Cox regression analysis within each zygosity by sex subset of the data. To allow for possible confounding effects of cardiopulmonary diseases, we conducted subgroup analyses as described in the previous section. Effects were quantified by the ratio of the death rates between the 2 groups. The differences in the distribution of comorbidity in the co-cases and the co-controls were tested in 2x2 tables for each diagnosis, using the χ² test. A value of P<0.05 was considered statistically significant. We used SAS (Cary, NC) version 9.14 and STATA (College Station, TX) version 11 software.

Results

Table 2 shows clinical characteristics of the study population. Table 3 shows the results from the Cox analyses. The co-cases showed a 20% increase in death rate compared with the co-controls (hazard ratio [HR], 1.20; 95% confidence interval [CI], 1.11–1.30; P<0.0001). When analyzing the data stratified by zygosity, we found that the increase in death rate was 30% (HR, 1.30; 95% CI, 1.09–1.55; P=0.003), 16% (HR, 1.16; 95% CI, 1.04–1.29; P=0.006), 20% (HR, 1.20; 95% CI, 0.97–1.47; P=0.093), and 23% (HR, 1.23; 95% CI, 0.92–1.64; P=0.169) for MZ, DZ same sex, DZ opposite sex, and unknown zygosity twins, respectively. In the analyses
Table 1. **International Classification of Disease Codes, Edition 8 to 10, Used for Classification of Lone AF Patients and Distribution of Comorbidity**

<table>
<thead>
<tr>
<th>Disease</th>
<th>ICD 10</th>
<th>ICD 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial fibrillation</td>
<td>I48</td>
<td>427.4</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>I20–22, I125</td>
<td>410–414</td>
</tr>
<tr>
<td>Valvular disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mitral valve disease</td>
<td>I05, I34</td>
<td>424.0, 394</td>
</tr>
<tr>
<td>Aortic valve disease</td>
<td>I06, I35</td>
<td>424.1, 395</td>
</tr>
<tr>
<td>Mitral and aortic valve disease</td>
<td></td>
<td>396</td>
</tr>
<tr>
<td>Other valvular disease</td>
<td>I07–08, I36, I137</td>
<td>424.9, 397</td>
</tr>
<tr>
<td>Hypertension</td>
<td>I10–13, I115</td>
<td>400–404</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>I42</td>
<td>425</td>
</tr>
<tr>
<td>Heart failure</td>
<td>I50</td>
<td>427.0, 427.1</td>
</tr>
<tr>
<td>Congenital cardiac malformation</td>
<td>Q20–24</td>
<td>746</td>
</tr>
<tr>
<td>Chronic obstructive lung disease</td>
<td>J44</td>
<td></td>
</tr>
<tr>
<td>Pulmonary heart disease</td>
<td></td>
<td>426</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>I26</td>
<td>450</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>I27</td>
<td></td>
</tr>
<tr>
<td>Chronic bronchitis</td>
<td></td>
<td>490–491</td>
</tr>
<tr>
<td>Emphysema</td>
<td></td>
<td>492</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>E10–11</td>
<td>250</td>
</tr>
<tr>
<td>Thyreotoxicosis</td>
<td>E05</td>
<td>242</td>
</tr>
</tbody>
</table>

ICD indicates International Classification of Disease.

stratified by sex, the male twins displayed a greater increase in death rate than the female twins through all zygosity groups. The increase in death rate was only statistically significant in MZ and DZ same sex twins and borderline significant in DZ opposite sex twins (MZ: HR, 1.36; 95% CI, 1.07–1.72; \( P=0.01 \); DZ same sex: HR, 1.22; 95% CI, 1.06–1.41; \( P=0.007 \); DZ opposite sex: HR, 1.35; 95% CI, 1.0–1.83; \( P=0.05 \); and unknown zygosity: HR, 1.44; 95% CI, 0.94–2.19; \( P=0.09 \)). The female MZ co-cases showed a borderline significant increase in death rate (HR, 1.26; 95% CI, 0.98–1.63; \( P=0.076 \)), whereas the female co-cases in all other groups of zygosity showed a trend toward increased death rates, which was not statistically significant.

When analyzing the survival of the co-twins of the twins with lone AF compared with the co-controls, we found a significant difference in death rate (HR, 1.21; 95% CI, 1.04–1.45; \( P=0.034 \)). This was most pronounced in MZ twins, but did not reach significance in the other zygosity groups. In the twins without heart failure and cardiomyopathy, we saw results similar to the analysis of the total twin population, with a significant increase in mortality (HR, 1.20; 95% CI, 1.09–1.33; \( P=0.0003 \)), which remained significant in both MZ and DZ same sex twins, although attenuating in the latter (Table 4).

Table 5 shows the distribution of comorbidity. There was a significantly higher prevalence of heart failure and cardiomyopathy in the co-cases, compared with the co-controls (18.5% versus 17.3%; \( P=0.0081 \) and 1.0% versus 0.5%; \( P=0.0138 \), respectively). There was no significant difference in the distribution of the other diagnoses.

### Discussion

In the present study, we have assessed the impact of having a sibling with AF on mortality. Overall, we found that the rate of death was 20% (11%–30%) higher in the group of twins with a co-twin diagnosed with AF compared with twins with an unaffected co-twin.

As MZ twins share nearly twice as much of their genetic material as DZ twins (≈100% versus ≈50%), we would expect an increase in mortality caused by common underlying genetic factors to be greater in the MZ than in DZ twins. In accordance with this, we found that the increase in death rate was almost doubled in MZ twins compared with DZ twins, suggesting the influence of genetic factors.

The increase in death rate can have several possible explanations. Studies on patients with implanted devices have shown that 38% to 81% of AF episodes are asymptomatic,31,32 and that asymptomatic AF is 12-fold more frequent than symptomatic events in patients with paroxysmal AF.33 Given the fact that AF is considered to be at least partially heritable,11 it is likely that a proportion of the twins with a co-twin diagnosed with AF might have undiagnosed and asymptomatic AF. It is well known that asymptomatic AF, in the same way as symptomatic AF, leads to increased mortality,34 and thus could be the cause of an increased death rate in the co-cases.

Studies have shown that AF also can be a manifestation in patients with inherited cardiac diseases resulting in more severe arrhythmias, such as the Brugada syndrome,17,35 long-QT syndrome,16,36,37 and familial dilated and hypertrophic cardiomyopathy.38,39 In 2009, Yang et al40 reported a mutation in the long-QT syndrome 1-gene \( KCNQ1 \) associated with familial AF, and a study from 2011 showed that 1 single mutation in this gene was capable of expressing both long-QT syndrome 1 and AF.41 These and similar findings suggest that variants in genes encoding ion channels involved in the cardiac action potential might contribute to the increased mortality rate in the co-cases.

We found that a male DZ twin, who has a co-twin with AF, has a higher increase in death rate than a female DZ twin with an affected co-twin. Male DZ twins with an affected female co-twin display one of the highest increases in estimated death rates (35% [95% CI, 0%–83%]). This might be the result of a difference in
susceptibility to genetic variation between men and women, suggesting that women might tolerate a higher degree of genetic variability than men before developing AF or other disease. Thus, it would require a greater number of genetic susceptibility variants for AF in the parental gene pool of a woman for her to develop AF than for a man. A DZ male twin with an affected female co-twin would, accordingly, be likely to carry a higher number of genetic variants increasing risk of disease and death, than a DZ female twin with an affected male co-twin. Our results from the analyses stratified by sex and zygosity support this hypothesis and are also in agreement with previous findings. The Framingham Heart Study showed that maternal AF increased the risk of AF in an individual <75 years 6-fold, compared with a 2.3-fold increase in paternal AF and that women with AF had a significantly higher increase in mortality compared with men (odds ratio, 1.5 for men and 1.9 for women). In 2008, Chen et al showed that women with lone AF had increased risk of having familial AF compared with men.

When analyzing the twins without heart failure and cardiomyopathy and the lone AF twins, we found similar effects on the rate of death, and the highest increase is seen in the MZ lone co-cases. These findings might be regarded supportive of the hypothesis of a greater genetic component in patients with lone AF, and it suggests that the increased mortality rate in the co-cases is not caused by confounding effects from other underlying partially heritable disease. However, the sample size in this group is small, and the true lone characteristics can be questioned.

The DZ twins do, in the same way as nontwin siblings, share 50% of their genes, and the prevalence of AF is similar in Denmark and other populations of European ancestry. This makes the findings regarding the DZ twins transferable to siblings in the general population, although one must take caution when comparing risks between different populations, especially of different ethnicity.

Limitations

Register-based studies are inherently limited and are regarded as good tools for generating hypotheses, that should, however, be replicated. There is an obvious lack of clinical data in the registers used in this study. We have only the diagnoses registered in the NPR, and no data on weight, height, blood pressure levels, medication, etc. We regard the internal validation of the data to be good, although there is a risk of misclassification. First, twins with a hospital diagnosis of AF before onset of registration of diagnoses in the LPR in 1977, and at no later stage, will not be identified as twins with AF in this study and could be misclassified

Table 3. Hazard Ratios From the Stratified Cox Regression Analyses of Co-cases and Co-controls, Including Analyses by Zygosity and Sex

<table>
<thead>
<tr>
<th>Zygosity</th>
<th>No. of Deaths/Total</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>All, born during and after 1912</td>
<td>4306/10790</td>
<td>1.20</td>
<td>1.11–1.30</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Monozygotic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>910/2174</td>
<td>1.30</td>
<td>1.09–1.55</td>
<td>0.003*</td>
</tr>
<tr>
<td>Men</td>
<td>438/924</td>
<td>1.26</td>
<td>0.98–1.63</td>
<td>0.076</td>
</tr>
<tr>
<td>Dizygotic SS</td>
<td>472/1250</td>
<td>1.36</td>
<td>1.07–1.72</td>
<td>0.012*</td>
</tr>
<tr>
<td>Women</td>
<td>2528/5343</td>
<td>1.16</td>
<td>1.04–1.29</td>
<td>0.006*</td>
</tr>
<tr>
<td>Men</td>
<td>1194/2415</td>
<td>1.10</td>
<td>0.94–1.28</td>
<td>0.232</td>
</tr>
<tr>
<td>Dizygotic OS</td>
<td>1334/2928</td>
<td>1.22</td>
<td>1.06–1.41</td>
<td>0.007*</td>
</tr>
<tr>
<td>Women</td>
<td>551/2624</td>
<td>1.20</td>
<td>0.97–1.47</td>
<td>0.093</td>
</tr>
<tr>
<td>Men</td>
<td>289/1715</td>
<td>1.10</td>
<td>0.82–1.46</td>
<td>0.536</td>
</tr>
<tr>
<td>Unknown zygosity</td>
<td>262/909</td>
<td>1.35</td>
<td>1.00–1.83</td>
<td>0.050</td>
</tr>
<tr>
<td>Women</td>
<td>317/649</td>
<td>1.23</td>
<td>0.92–1.64</td>
<td>0.169</td>
</tr>
<tr>
<td>Men</td>
<td>176/328</td>
<td>1.07</td>
<td>0.71–1.60</td>
<td>0.750</td>
</tr>
<tr>
<td></td>
<td>141/321</td>
<td>1.44</td>
<td>0.94–2.19</td>
<td>0.091</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; OS, opposite sex; and SS, same sex.
*Statistically significant, P<0.05.

Table 4. Hazard Ratios From the Stratified Cox Regression Analyses of the Subsets of Twins Without Heart Failure and Cardiomyopathy and Twins With Lone AF

<table>
<thead>
<tr>
<th>Zygosity</th>
<th>No. of Deaths/Total</th>
<th>HR</th>
<th>95% CI</th>
<th>P</th>
<th>No. of Deaths/Total</th>
<th>HR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>All, born during and after 1912</td>
<td>2796/7749</td>
<td>1.20</td>
<td>1.09–1.32</td>
<td>0.0003*</td>
<td>756/2691</td>
<td>1.21</td>
<td>1.01–1.45</td>
<td>0.034†</td>
</tr>
<tr>
<td>Monozygotic</td>
<td>576/1551</td>
<td>1.31</td>
<td>1.06–1.62</td>
<td>0.014†</td>
<td>189/603</td>
<td>1.45</td>
<td>1.02–2.06</td>
<td>0.038†</td>
</tr>
<tr>
<td>Dizygotic SS</td>
<td>1577/3652</td>
<td>1.14</td>
<td>1.00–1.30</td>
<td>0.048†</td>
<td>397/1200</td>
<td>1.07</td>
<td>0.83–1.37</td>
<td>0.619</td>
</tr>
<tr>
<td>Dizygotic OS</td>
<td>428/2074</td>
<td>1.25</td>
<td>0.99–1.57</td>
<td>0.064</td>
<td>117/754</td>
<td>1.22</td>
<td>0.79–1.88</td>
<td>0.368</td>
</tr>
<tr>
<td>Unknown zygosity</td>
<td>215/472</td>
<td>1.19</td>
<td>0.84–1.69</td>
<td>0.336</td>
<td>53/134</td>
<td>1.34</td>
<td>0.67–2.70</td>
<td>0.406</td>
</tr>
</tbody>
</table>

No HF twins denotes twins whose co-twins did not have a diagnosis of heart failure or cardiomyopathy. Lone AF twins denotes twins whose co-twin did not have a diagnosis of cardiopulmonary or endocrine disorders before or within 2 years of the diagnosis of AF.
AF indicates atrial fibrillation; CI, confidence interval; HF, heart failure; OS, opposite sex; and SS, same sex.
*Statistically significant, P<0.05.
as controls. This also applies for patients who were diagnosed as outpatients before 1995 and not at a later stage. Combined with the fact that the prevalence of AF increases with increasing age, this could result in an underestimation of the number of co-cases in the earliest birth cohorts. Second, false-positive diagnoses of AF would lead to inflation of the number of co-twins included as co-cases. We have sought to minimize misclassification by excluding twins born before 1912, resulting in a maximum age of 65 years at the time of onset of registration in the NPR. Moreover, the AF diagnosis has been found to be valid, with <5% misclassification. Third, the diagnosis of lone AF was made based on data from the NPR as a proxy for a clinical diagnosis. However, none of the diagnoses used to define lone AF (Table 1) have been validated, and the lack of clinical data further weakens this definition. The misclassification because of invalid diagnoses could result in under- as well as overestimation of the number of twins with lone AF and makes this estimate uncertain.

Several diseases that are known to cause AF have also been associated with genetic variants (insulin- and non-insulin-dependent diabetes mellitus, hypertension, cardiomopathy). The prevalence of these diseases could be a confounder in this study. AF could in this case be secondary to an underlying partially heritable disease, and the increase in death rates in the co-cases could be explained by a higher mortality because of the primary disease and not because of an inherited susceptibility to arrhythmia. We have attempted to address this by assessing the prevalence of diseases known to predispose to AF in the populations and by doing subgroup analyses on twins without heart failure and cardiomopathy and twins with lone AF. Although we found that heart failure and cardiomopathy are slightly more prevalent in the co-cases, most of the diseases were evenly distributed in the 2 groups, and the increased mortality in the co-cases remained significant in both subgroup analyses.

Conclusions

In this study, we found that twins with a co-twin diagnosed with AF had a 20% increased death rate compared with twins with an unaffected co-twin, and that male twins with affected female co-twins displayed the largest increase in mortality. The effect on mortality was similar when analyzing twins without heart failure and cardiomopathy or with lone AF, suggesting that it is not a result of confounding risk factors. Our findings indicate that co-twins of twins with AF may have a genetic susceptibility to cardiac arrhythmias and that we should put more emphasis on early detection of AF and other arrhythmias in these persons. Additionally, our findings suggest that women with AF may have a greater genetic component than men with AF.

Sources of Funding

This work was supported by grants from The Memorial Fund of Eva and Henry Frøelck; Dagmar Marshalls Fond; Aase og Egjar Danielsen’s Fond; The John and Birthe Meyer Foundation; The Research Foundation at the Heart Center, Copenhagen University Hospital; The Danish National Research Foundation Center for Cardiac Arrhythmia (DARC), Fondsbyrøkselsleren Henry Hansen og Hustru Karla Hansen, fstd Westergaards Legat; Arvid Nilsson Foundation; and Odd Fellow’s Medical Scientific Research Foundation, Norway. The Danish Aging Research Center is supported by a grant from the VELUX Foundation.

Disclosures

None.

References

Familial Atrial Fibrillation Predicts Increased Risk of Mortality: A Study in Danish Twins
Ingrid Elisabeth Christophersen, Esben Budtz-Jørgensen, Morten S. Olesen, Stig Haunsø, Kaare Christensen and Jesper Hastrup Svendsen

*Circ Arrhythm Electrophysiol.* 2013;6:10-15; originally published online December 19, 2012; doi: 10.1161/CIRCEP.112.971580
*Circulation: Arrhythmia and Electrophysiology* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-3149. Online ISSN: 1941-3084

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