Development of permanent atrial fibrillation in patients with dual-chamber pacemaker

Authors: Maciej Dębski, Mateusz Ulman, Andrzej Ząbek MD, Krzysztof Boczar, Kazimierz Haberka, Marcin Kuniewicz, Jacek Lelakowski, Barbara Małecka

Article type: Original article

Received: June 12, 2019.

Accepted: September 16, 2019.

Published online: September 17, 2019.

ISSN: 0022-9032

e-ISSN: 1897-4279

This is an Open Access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives 4.0 International License (CC BY-NC-ND 4.0), allowing third parties to download articles and share them with others, provided the original work is properly cited, not changed in any way, distributed under the same license, and used for noncommercial purposes only. For commercial use, please contact the journal office at kardiologiapolaska@ptkardio.pl.
Development of permanent atrial fibrillation in patients with dual-chamber pacemaker

Maciej Dębski¹ MD, Mateusz Ulman¹ MD, Andrzej Ząbek¹ MD, PhD, MSc, Krzysztof Boczar¹ MD, PhD, Kazimierz Haberka¹ MD, Marcin Kuniewicz¹,² MD, PhD, Jacek Lelakowski¹,³ MD, PhD, Barbara Małecka¹,³ MD, PhD

1 – Department of Electrocardiology, John Paul II Hospital, Kraków, 31-202, Prądnicka 80, Poland
2 - Department of Anatomy, Jagiellonian University Medical College, Kraków, 31-034, Mikołaja Kopernika 12, Poland
3 - Institute of Cardiology, Jagiellonian University Medical College, Kraków, 31-202, Prądnicka 80, Poland

Corresponding author: Andrzej Ząbek MD, PhD, MSc
Department of Electrocardiology, John Paul II Hospital, Kraków, 31-202, Prądnicka 80, Poland
tel: (+48) 126142381, fax: (+48) 126332399.
Email: andrzej_j_z@poczta.onet.pl

Acknowledgements: None
Funding: None
Conflict of interest: None
Short title: Dual-chamber pacing and permanent atrial fibrillation development
Abstract

Background: Atrial fibrillation (AF) is thought to be a progressive arrhythmia. The impact of gender and position of right ventricular (RV) lead is not well recognized. Whilst non-paroxysmal AF compared to paroxysmal has been associated with increased mortality in general population, its predictive value on survival in dual-chamber pacemaker patients is less clear.

Aims: We sought to determine the incidence of permanent AF in a cohort with dual-chamber pacemaker, analyse the effect of selected baseline characteristics on permanent AF development and examine its impact on patients’ survival.

Methods: Retrospective cohort study comprised of 3932 consecutive patients who underwent DDD pacing system implantation between 1984 and 2014. Follow-up was completed in August 2016. We included 3771 (96%) patients with post-operative follow-up and known vital status. Occurrence of permanent AF and all-cause mortality were the study end-points.

Results: During mean follow-up of 6.5 years, permanent AF occurred in 717 (19%) patients. Gender (HR 1.316, 95% CI 1.134–1.528, for male), increasing age at implant (HR 1.041, 95% CI 1.033–1.049, per year), history of AF (HR 3.521, 95% CI 3.002–4.128) were independently associated with permanent AF development whereas position of RV lead (apical versus non-apical) and primary pacing indication (atrioventricular block versus sick sinus syndrome) were not related to permanent AF. Occurrence of permanent AF was a significant risk factor for increased mortality (age- and sex-adjusted HR 1.475, 95% CI 1.294–1.682).

Conclusions: Increasing age, male gender and pre-existing AF independently predicted permanent AF development. Occurrence of permanent AF was significantly associated with reduced survival.

Key words: atrial fibrillation; gender; mortality; pacing
What’s New?

The study revealed that male gender compared to female gender along with history of atrial fibrillation and increasing age were associated with increased risk of permanent atrial fibrillation development. On the other hand, position of right ventricular lead and primary pacing indication did not influence the occurrence of permanent atrial fibrillation. Furthermore, we demonstrated that in patients with dual-chamber pacemaker permanent atrial fibrillation resulted in a significant reduction of survival.

Introduction

Atrial fibrillation (AF) is the most commonly encountered arrhythmia in the population and has been referred to as “epidemic” affecting approximately 3% of adults [1]. AF is considered to be a progressive arrhythmia. In many patients it starts with short, infrequent attacks and over time progresses to longer and more frequent episodes. In minority of patients AF remains paroxysmal over long time or may even regress. In majority of patients, however, the burden of AF increases and becomes sustained. Persistent, long-standing AF is diagnosed if rhythm control strategy is adopted and permanent AF when no interventions are undertaken to revert it to sinus rhythm [2]. Importantly, chronic AF precludes the use of dual-chamber pacing due to inability to pace the atrium.

It is well established across many populations that AF is a risk factor for increased mortality [3-8]. Of note, in our recent study we demonstrated that pre-implant AF was not associated with reduced survival in consecutive dual-chamber pacemaker (DDD PPM) recipients [9]. A retrospective analysis of patients implanted with modern DDD PPM capable of storing AF data showed that AF burden was not predictive of mortality [10]. On the other hand, recent
real world community-based cohort study and a meta-analysis involving six large-scale randomized controlled trials on oral anticoagulation therapy demonstrated that patients with persistent or permanent AF compared to paroxysmal AF had significantly higher risk of all-cause mortality [11,12]. In addition, the associations between development of permanent AF and baseline variables such as pacing indication, gender and position of the right ventricular (RV) lead remain unclear. Previous reports suggested that the natural history of AF was affected by the cumulative percentage of atrial and ventricular pacing therefore outcomes in general populations may not be applicable to dual-chamber paced cohorts [10,13]. We sought to determine risk factors favouring development of permanent AF and assess its affect on long-term survival in a large DDD paced cohort.

**Methods**

The study cohort consisted of all consecutive patients who underwent de novo DDD PPM implantation between 4th October 1984 and 31st December 2014 at a high-volume, third-level reference university cardiology centre. Patients were followed until 31st August 2016 or death, whichever came first. The data on patients’ vital status and dates of death was collected from the national death registration system after the completion of follow-up period. The survival and lead-related complications in the present cohort have been studied previously [9,14,15]. The end-points were onset of permanent AF and all-cause mortality. The data used in the analysis included (1) patients’ demographic baseline characteristics: age at implantation and sex; (2) index arrhythmia (primary electrocardiographic pacing indication): AVB or SSS; (3) history of AF prior to DDD PPM implantation; (4) position of the RV lead: apical or non-apical at discharge from the department; (5) time of permanent AF onset and (6) date of death declared in the death certificate. This information was retrospectively gathered from the paper and electronic medical records from hospital
admissions, operative reports and cardiology clinic visits including pacemaker checks. We retrospectively reviewed device interrogation reports, electrocardiograms (ECG) and Holter ECG recordings from inpatient and outpatient encounters. Patients had standard device interrogation follow-up approximately 3 months after implantation followed by every 6–12 months thereafter. We did not distinguish between atrial fibrillation and atrial flutter. Pre-implant AF was defined as AF documented on an ECG prior to DDD PPM implantation and included paroxysmal and persistent AF provided that the restoration of sinus rhythm was planned after implantation. Patients with permanent AF were routinely implanted with single-chamber VVI PPM throughout the study period. We used 2016 ESC Guidelines to define permanent AF [2]. In a present study the minimum of two consecutive visits were required to diagnose permanent AF, with no interim documented sinus rhythm or further evidence of sinus rhythm until the end of the study or the patient's death. Moreover, it was a prerequisite that the DDD mode was reprogrammed to ventricular based pacing prior to or at the end of follow-up. The time of permanent AF onset was defined as the first instance when AF was detected and at the end of follow-up fulfilled the above-mentioned criteria.

Statistical analysis

Data were analysed using IBM SPSS Statistics Version 25.0 software (IBM Corp., Armonk, N.Y., USA). Continuous variables are expressed as mean (SD) plus median and interquartile range (IQR) if not normally distributed. Normal distribution was tested with Kolmogorow–Smirnow test with Lillefors adjustment. Continuous variables were compared by means of Mann–Whitney U test. Categorical variables were compared using the Pearson’s $\chi^2$ test. The proportion of patients who progressed to permanent AF was calculated by the Kaplan–Meier method. Mortality rates between study cohort and patients lost to follow-up were compared with log-rank test. Proportional hazards Cox regression analysis was used to determine the association between selected baseline variables and permanent AF development. We assessed
the effect of time-covariate interaction to test the validity of the proportional hazards. Cox regression with time-dependent covariate was used to assess the association between permanent AF occurrence and post-implant survival and subsequently to explore potential subgroup effects [16]. A $P$-value $<0.05$ was considered statistically significant.

Results

Between 4 October 1984 and 31 December 2014 a total of 3932 consecutive patients underwent de novo DDD PPM implantation. We excluded 4 patients whose vital status as of the end of follow-up was unknown and 157 patients who did not attend pacemaker clinic prior to follow-up completion. Comparison of patients who were lost to follow-up after initial DDD PPM implantation with patients who remained in the follow-up is presented in Table 1. The remaining 3771 patients and a total of 24431.8 patient-years of follow-up were analysed. Women accounted for 46.7% of patients. Mean (SD) device follow-up was 6.5 (5.2), median 5.2, IQR 6.5, max. 30.8 years. We analysed in total 29,581 post-implant encounters in which device parameters, electrogram and ECG were obtained; mean (SD) 7.8 (6.4), median 5, IQR 8. The mean (SD) survival time (e.g. until patients’ death or study follow-up completion) was 7.8 (5.3), median 6.5, IQR 6.8, max. 31.3 years. AF prior to DDD pacemaker implantation was detected in 1276 (34%) patients. Patients with pre-existing AF compared to patients without AF were statistically significantly older [mean (SD) age at implantation, 71.8 (10), median 73, IQR 11.9 versus 68.8 (12.9), median 71.3, IQR 15.3 years, $P <0.001$], more frequently female (56% versus 42%, $P <0.001$) and had higher prevalence of SSS relative to AVB (84% versus 58%, $P <0.001$).

During the entire follow-up 717 (19%) patients developed permanent AF in a mean (SD) period of 4.6 (4.1), median 3.6, IQR 5.4 years. At 1, 5, 10 and 15-year period after implant 4.4%, 13.3%, 25%, 32.3% of patients had permanent AF, respectively (Figure 1).
Comparison of patients with permanent AF versus patients without permanent AF in the total cohort is presented in Table 2. Additionally, the comparison of patients who underwent DDD PPM during the last decade of the inclusion period (2005-2014) assessing differences in baseline characteristics between patients who developed permanent AF versus non-permanent AF patients is presented in Table 3.

In the total cohort, male gender was associated with significantly higher risk of permanent AF development compared to women, hazard ratio (HR) 1.316, 95% confidence interval (CI) 1.134–1.528, P <0.001. Increasing age at implant (HR 1.041, 95% CI 1.033–1.049, P <0.001, per year), history of AF (HR 3.521, 95% CI 3.002–4.128, P <0.001) were the independent predictors for permanent AF occurrence. The position of RV lead and pacing indication were not associated with permanent AF (Figure 2). The additional Cox regression analysis on 2475 patients who had DDD PPM implantation during the last decade replicated the findings of the entire cohort analysis (Figure 3).

In terms of mortality, 310 (43%) patients with permanent AF died after a mean (SD) period of 4.6 (3.6), median 3.9, IQR 5.5, maximum 17.3 years following the onset of permanent AF. In the group without permanent AF 1032 (32%) patients died after mean (SD) 6.2 (5.0), median 4.9, IQR 6.7 years following first implantation. During the exposure to permanent AF the rate of death was 85 per every 1,000 patient years whereas during non-exposure to permanent AF the rate of death was 40 per every 1,000 patient years of a study. Cox proportional hazards model with time-varying covariate confirmed that occurrence of permanent AF significantly increased mortality during follow-up (HR = 1.885, 95% CI 1.654–2.148, P <0.001). The observed effect remained statistically significant after adjustment for age at implantation and sex (HR = 1.475, 95% CI 1.294–1.682, P <0.001). The association was consistently observed in patients selected with regard to gender (men: HR = 1.841; women: HR = 1.932), index arrhythmia (AVB: HR = 2.190; SSS: HR = 1.796), history
of AF (yes: HR = 1.401; no: HR = 2.486) and position of RV lead (apical: HR = 1.924; non-apical: HR = 1.768) (Table 4).

**Discussion**

**Epidemiology of permanent AF in DDD paced population**

This study demonstrates that the incidence of permanent AF development during a mean of 6.5 years of follow-up reached 19%. The percentage of patients with pre-implant AF at baseline amounted to 34%. Our findings accord with previous prospective and retrospective reports. In paced populations, the incidence of chronic AF was several times higher than in non-paced patients and could be estimated at 1.6% to 3.8% per year, and from 15% to 20% as a cumulative lifetime incidence [17,18]. In prospective analyses undertaken predominantly in patients with sinus node dysfunction implanted with DDD PPM, the rate of pre-implant AF was between 36% and 63% [17,19-21] whereas the incidence of permanent AF was estimated at 8% to 15.2% after a mean period of follow-up from 1.7 to 5.4 years [17,19-22]. Skanes et al. in the prospective trial reported the rate of chronic AF in DDD pacemaker population at 2.8% per year [23]. In retrospective studies analysing permanent AF development, such an end-point was noted in the range from 6.4% to 22% of patients after a mean follow-up from 2.7 to 7 years [24-26]. Noteworthy, Konieczyńska et al. demonstrated worryingly low awareness of the arrhythmia symptoms and its progressive nature among patients with AF and with or without a cardiac device. Only about one third of patients who were surveyed in a tertiary cardiology centre perceived AF as a progressive disease and a similar proportion of patients knew that AF may not always be symptomatic. Other significant knowledge gaps were identified with regard to treatment and complications [27]. Furthermore, authors found that knowledge of AF symptoms and its progressive course was significantly worse in patients from a small volume district hospital compared to peers from a tertiary cardiology
centre [28]. An essential and relevant education may be provided to the subgroup of patients with AF and a pacemaker at the regular device follow-up visits.

**Risk factors for permanent AF development**

In terms of gender, prevalence and incidence of AF across all age groups is higher in men than in women [1,8,29-31]. In 2010 the prevalence rates were 596 in men and 373 in women and incidence rates were 76 in men and 60 in women, per 100,000 people [30]. After adjustment for age and other risk factors, men had a 1.5 to 2 times greater risk of developing AF than women [32,33]. However, because women live longer than men and AF increases in prevalence with age, the absolute number of women with AF exceeds that of men. Potpara et al. reported that paroxysmal AF was at baseline more prevalent in females than in males [34], in a similar way to our results. Noteworthy, recent meta-analysis including six large randomized controlled trials on non-vitamin K oral anticoagulation demonstrated that patients with paroxysmal AF were more likely to be female compared to patients with persistent or permanent AF [12]. Unexpectedly, we found that male gender was associated with increased risk of permanent AF development. Studies on non-pacemaker populations have not identified gender-related difference with regard to permanent AF development [34-36]. On the other hand, Veasey et al. showed that in patients with DDD PPM and paroxysmal AF, male gender was significantly associated with progression to persistent or permanent AF in univariate model, but it was not found to be independently significant on multivariate analysis [10].

In the current study, age at baseline was associated with permanent AF development. It is well recognized that age increases the incidence of AF. Age was demonstrated as independent factor for AF occurrence and chronic permanent AF development in numerous previous studies [5,8,22,25,29,31,35-38]. The odds ratio (OR) of atrial fibrillation for each decade of advancing age was 2.1 for men and 2.2 for women [22].
In our population patients with a history of AF had more frequently SSS compared to AVB. It is consistent with findings of Alonso et al. who estimated that in patients with SSS the incidence rate of AF was ten times higher than in the normal population [39]. In accordance with our findings, a history of AF before pacemaker implantation was the strongest independent predictor of post-implant AF occurrence in both prospective [17] and retrospective studies [25,26,37,38].

To our knowledge, no randomised large-scale clinical studies have demonstrated so far a more deleterious clinical long-term effect of the RV apical pacing compared with septal pacing in bradycardia pacemaker recipients with normal baseline left ventricular function. A randomised trial comparing sustained apical RV pacing with septal pacing in patients with high-grade AVB failed to demonstrate any difference in AF burden over a 2-year study period [40]. Of note, retrospective study involving 477 consecutive patients who underwent PPM implantation for complete or advanced AVB demonstrated that pacing in Hisian area compared to apical and septal was associated with lower risk of persistent/permanent AF occurrence after mean follow-up of nearly 5 years [38]. Importantly, the reported risk of chronic AF development was similar in both apical and septal groups with the rate of progression at 25.7% and 28%, respectively [38]. In keeping with these findings, we found that the risk of permanent AF development was similar between patients with apical and non-apical RV lead position. Moreover, the analysis on patients who had DDD PPM implanted during the last decade of the inclusion period showed similar results.

**Mortality**

In subjects aged 55-94 years from the original cohort of the Framingham study, the presence of AF was independently associated with a 1.5-fold increased the risk of death in men and 1.9-fold increased risk of death in women [4]. Consequently, the presence of AF limited the advantage that women have over men in regard to longevity [4]. Other authors also observed
that AF was associated with increased mortality risk as compared with counterparts without AF, even after accounting for other comorbidities [3,7]. Subjects with incident AF had a 3.5-fold higher risk of death compared to those without AF according to work of Magnussen et al. [5]. Interestingly, in our previous analysis on the association between baseline factors and long-term mortality we did not find significantly increased mortality in patients with DDD PPM and pre-implant AF compared to patients without a history of AF at baseline [9]. On the other hand, in the present study we confirmed that permanent AF was associated with an unfavourable effect on long-term survival. It accords with the analysis of Polewczyk et al. who showed that permanent AF was associated with significantly higher mortality following transvenous lead extraction in the mean follow-up of 3.7 years [41]. Additionally, our findings are in line with recent reports based on general population showing that permanent AF was a predictive factor for mortality compared to paroxysmal AF. In a real world community-based cohort study the progression to permanent AF was an independent risk factor for death or hospital admission [11]. The observation that patients with persistent or permanent AF compared to paroxysmal AF have significantly higher risk of all-cause mortality was validated in the recent meta-analysis involving six large-scale randomized controlled trials on oral anticoagulation therapy and a total of 70,447 AF patients [12].

**Study limitations**

Our observations should be interpreted in the context of limitations imposed by a retrospective study design. We did not take into account patients’ comorbidities, medications, baseline echocardiographic parameters at index procedure and we did not track subsequent conducted cardioversions, AF ablations and changes during follow-up in incident comorbidities, medicine prescribing, echocardiographic parameters and device reprogramming, all of which might have influenced the permanent AF occurrence. Primary reason was the missing data due to patients’ cardiology follow-up in local centres and
destruction of paper patient records following the 20-year retention period. Additionally, clinical risk factors are dynamic in nature as for instance elderly patients accumulate comorbidities, atrial and ventricular pacing percentage is frequently changing depending on device programming and medications. In light of the foregoing considerations, we chose to base our analysis on static baseline risk factors and complete data for the entire population.

Another limitation was the lack of continuous cardiac rhythm monitoring. The diagnosis of permanent AF was mostly based on standard intermittent monitoring techniques during pacemaker checks. Pacemakers equipped with automated storage of intracardiac electrocardiograms and AF diagnostic capabilities were not available for more than a half of the 30-year study enrolment. Hence, it is plausible that considerable percentage of our patients with conventionally defined permanent AF might have spontaneously reverted into sinus rhythm between yearly follow-up visits and in fact remained in paroxysmal or persistent form of AF [10,42].

**Conclusions**

Our data reveal several important findings such as the increased risk of permanent AF development in men and confirmed the association with increasing age and history of pre-implant AF. On the other hand, the position of RV lead and type of pacing indication were not related to permanent AF occurrence. Importantly, these results remained unchanged when only the last decade of implantation period was analysed. Furthermore, current study showed increased mortality in patients with permanent AF compared to patients without permanent AF.
References


Table 1. Comparison of patients with and without post-discharge follow-up

<table>
<thead>
<tr>
<th>Factor</th>
<th>Lost to follow-up</th>
<th>Remained in follow-up</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>157 (4)</td>
<td>3771 (96)</td>
<td></td>
</tr>
<tr>
<td>Age at implantation, mean (SD), median, IQR [years]</td>
<td>70.3 (12.7)</td>
<td>69.8 (12.1)</td>
<td>0.85</td>
</tr>
<tr>
<td></td>
<td>71.8, 13.9</td>
<td>71.9, 14.2</td>
<td></td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>56 (36)</td>
<td>1761 (47)</td>
<td>0.007</td>
</tr>
<tr>
<td>SSS indication, n (%)</td>
<td>83 (53)</td>
<td>2527 (67)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pre-implant AF, n (%)</td>
<td>42 (27)</td>
<td>1276 (34)</td>
<td>0.07</td>
</tr>
<tr>
<td>RV lead at apex, n (%)</td>
<td>68 (43)</td>
<td>1625 (43)</td>
<td>0.96</td>
</tr>
<tr>
<td>All-cause mortality, n (%)</td>
<td>93 (59)</td>
<td>1342 (36)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 2. Comparison of baseline characteristics in patients with and without permanent atrial fibrillation in the entire cohort

<table>
<thead>
<tr>
<th>Factor</th>
<th>Permanent atrial fibrillation</th>
<th>No permanent atrial fibrillation</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>717 (19)</td>
<td>3054 (81)</td>
<td></td>
</tr>
<tr>
<td>Age at implantation, mean (SD), median, IQR [years]</td>
<td>71.4 (9.1)</td>
<td>69.4 (12.7)</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>71.9, 11.7</td>
<td>71.9, 15.1</td>
<td></td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>344 (48)</td>
<td>1417 (52)</td>
<td>0.45</td>
</tr>
<tr>
<td>Sick sinus syndrome indication, n (%)</td>
<td>551 (77)</td>
<td>1976 (23)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Factor</td>
<td>Permanent atrial fibrillation</td>
<td>No permanent atrial fibrillation</td>
<td>(P)</td>
</tr>
<tr>
<td>------------------------------------</td>
<td>------------------------------</td>
<td>---------------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>n (%)</td>
<td>368 (15)</td>
<td>2107 (85)</td>
<td></td>
</tr>
<tr>
<td>Age at implantation, mean (SD), median, IQR [years]</td>
<td>74.1 (8.4) 75.5, 11.1</td>
<td>71.6 (11.8) 73.9, 13.4</td>
<td>0.003</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>178 (48)</td>
<td>1007 (48)</td>
<td>0.84</td>
</tr>
<tr>
<td>Sick sinus syndrome indication, n (%)</td>
<td>288 (78)</td>
<td>1327 (63)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pre-implant atrial fibrillation, n (%)</td>
<td>255 (69)</td>
<td>703 (33)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Right ventricular lead at apex, n (%)</td>
<td>67 (18)</td>
<td>298 (14)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Table 3. Comparison of baseline characteristics among patients who underwent implantation between 2005-2014
Table 4. Association between the permanent atrial fibrillation occurrence and survival after dual-chamber implant; subgroup analysis

<table>
<thead>
<tr>
<th>Factor</th>
<th>Hazard ratio</th>
<th>95% confidence interval</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age at implant</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;70</td>
<td>2.150</td>
<td>1.705 – 2.712</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≤70</td>
<td>1.403</td>
<td>1.227 – 1.668</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1.932</td>
<td>1.590 – 2.348</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male</td>
<td>1.841</td>
<td>1.543 – 2.196</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Sick sinus syndrome indication</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.796</td>
<td>1.543 – 2.093</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No</td>
<td>2.190</td>
<td>1.699 – 2.824</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Pre-implant atrial fibrillation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1.401</td>
<td>1.132 – 1.734</td>
<td>0.002</td>
</tr>
<tr>
<td>No</td>
<td>2.486</td>
<td>2.090 – 2.958</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Right ventricular lead position</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apical</td>
<td>1.924</td>
<td>1.641 – 2.256</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non-apical</td>
<td>1.768</td>
<td>1.404 – 2.226</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Figure 1. Occurrence of permanent atrial fibrillation during the study period

Figure 2. Association of baseline factors with permanent atrial fibrillation development after dual-chamber pacemaker implantation in the entire cohort
Figure 3. Association of baseline factors with permanent atrial fibrillation development in group of patients who underwent implantation between 2005-2014