Mortality in patients with atrial fibrillation has significantly decreased during the last three decades: 35 years of follow-up in 1627 pacemaker patients

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Aim The impact of atrial fibrillation (AF) on mortality is not fully understood. We therefore sought to investigate long-term effects of AF on mortality in patients with the need for pacemaker (PM) therapy.

Methods and results A total of 1627 PM recipients with AF at implantation were followed in a single-centre, longitudinal study for up to 35 years. Baseline factors affecting survival and long-term follow-up were analysed. A total of 7362 patient-years of follow-up (PM implanted between 1971 and 2000, followed until 31 December 31 2005) were analysed. Female PM recipients lived significantly longer than male (P = 0.025; mean survival 91.9 vs. 72.1 months) despite older age at time of inclusion. Mean survival times almost doubled for patients implanted in the last decade, with 139.8 months in the nineties vs. 66.8 months in the seventies and 75.7 months in the eighties (P < 0.001). Male gender, age at implantation, non-syncopal bradycardia, and decade of implantation influenced survival.

Conclusion Life expectancy in AF patients after PM implantation has doubled within the last three decades, with a mean survival in the overall population of 7.6 years for women and 6.0 years for men. Survival is influenced by several simple baseline characteristics, which may help to identify patients with very long survival times.

KEYWORDS Atrial fibrillation; Pacemaker; Mortality

Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia with a prevalence of up to 9% in octogenarians.1 Risk factors that predispose to the development of AF have been widely defined and include male gender, age, hypertension, congestive heart failure, and valve disease.2 As prevalence of AF increases and therapeutic approaches become more invasive, the issue of mortality among this population has to be addressed. Evidence suggests that AF is independently associated with mortality in certain clinical subsets, such as acute coronary syndrome3 and congestive heart failure.4,5 Postoperative AF after coronary artery bypass surgery6 or esophagectomy7 also predicts worse outcome. Data from the Framingham Heart Study also provides evidence for an excess mortality in AF patients independent of other risk factors,8 a finding that even seems to be true for patients with idiopathic AF.9 However, most of these data are limited to certain clinical subsets, have been collected many years ago or do not provide long-term follow-up.

Mortality rates of AF patients with pacemaker (PM) implantation have not been systematically investigated. Evidence from our own patient population suggests a higher mortality when the index arrhythmia leading to PM implantation was AF.10 To analyse factors that influence long-term survival in this subset of our population, we analysed data from 1627 patients with AF at the time of PM implantation.

Methods

Subjects

Between 1 January 1971 and 31 December 2000, 6502 patients received a PM in the Department of Cardiology of the University Hospital Freiburg in Germany and are stored in our local database. A total of 1627 patients with AF as the index arrhythmia were followed until 31 December 2005. Clinical data included are gender,
age, date of implantation, baseline ECG characteristics (rhythm, QRS width, type of bundle branch block), and symptoms leading to implantation. Symptoms were classified as (i) syncope (Morgagni-Adam-Stokes) with brief loss of consciousness, (ii) near-syncope with dizziness or vertigo associated with bradycardia, and (iii) asymptomatic bradyarrhythmia, i.e. significant, documented bradycardia/pauses without associated symptoms (usually Holter-monitoring documented bradycardia and/or pauses).

The type of PM and the programming were left to the discretion of the treating physician, but were based on the recommendation of the AHA, the ESC, and the German Cardiac Society current at the time of implantation. Patients were categorized into three decades according to the date of implantation of their first PM: 1971–1980 (the seventies, D1); 1981–1990 (the eighties, D2), and 1991–2000 (the nineties, D3). Endpoint of the study was all-cause mortality.

Patients with AF at the time of implantation (n = 1627, 25.0% of the total PM population) were included in this study and followed in our outpatient clinic in standardized 6–12 months intervals. For those missing an appointment, a telephone follow-up was performed, and, if appropriate, date and cause of death was obtained from the patient’s physician. If telephone follow-up did not yield sufficient information, patients were characterized as ‘lost for follow-up’ on the day of their last visit.

Statistical analysis
Data are presented as means ± SD. Comparisons between groups were performed using a Student’s t-tests, Mann-Whitney’s tests, or χ²-tests, where appropriate. Survival probabilities were estimated by the Kaplan–Meier method. The influence of age and gender on long-term survival is depicted in Figure 1. The assumption of proportionality of the Cox models was verified by visual inspection of the log survival plots. Results of the Cox models are presented as relative risk ratios with 95% confidence intervals together with the P-values from Wald’s tests. All test of significance were two-sided and a P-value of < 0.05 was considered statistically significant. For comparisons of more than two groups, a closed test procedure was applied testing overall effects first followed by pairwise tests if the overall test was significant. Therefore, no further adjustment was made for multiple testing. Statistical analysis was performed using SAS (SAS Institute, Cary, NJ, USA) and Graphpad Prism (Version 4; Graphpad Inc., San Diego, CA, USA).

Results
In 1627 of 6502 patients (25.0%) stored in our database, the primary rhythm disorder leading to PM implantation was AF with severe and/or symptomatic bradycardia. Of these patients, 886 (54.5%) were male, 95.9% received a VVI device. We analysed a total of 7362 patient-years of follow-up. During the study, 753 patients (46.3%) died. Baseline patient characteristics are summarized in Table 1.

With a mean follow-up of 54.0 ± 58.7 months (median follow-up 34.3 months, interquartile range 75.6), the median patient survival was 85.4 months (~7.1 years). At 5, 10, 15, and 20 years after implantation 58.5, 39.0, 24.8, and 17.3% patients, respectively, were still alive.

Long-term survival during three decades
In D1, D2, and D3, we included 571, 676, and 380 patients, respectively. Mean age at implantation was in D1 72.3 years, in D2 74.2 years, and in D3 75.7 years (P < 0.01). Despite increasing age, patients implanted in the last decade had a significant benefit in terms of survival (Figure 1). Mean survival time was 66.8 months in D1, 75.7 months in D2, and 139.8 months in D3. Survival time in D3 was significantly longer than in D1 (P < 0.001) and D2 (P < 0.005) with 5 (10/15) year survival rates of 54.8% (35.0/20.9%), 57.3% (37.6/23.8%), and 67.4% (51.6/38.4%) of those implanted in D1, D2, and D3, respectively. These effects were evident in all age groups.

Age and gender differences in survival
The influence of age and gender on long-term survival is shown in Figures 2 and 3, respectively. Mean age at implantation in the overall study population was 73.9 ± 9.2 years. As expected, survival times decreased with increasing age with median survival times for patients aged ≤ 60 years: 16.8 years, patients aged 61–70 years: 10.3 years, patients aged 71–80 years: 6.4 years, and > 80 years: 3.9 years (P < 0.0001; Figure 2).

Female PM recipients were significantly older at the time of inclusion (74.4 ± 8.7 vs. 73.5 ± 9.4 years, P < 0.05), but lived significantly longer than male (P < 0.01; median survival 91.9 vs. 72.1 months; Figure 3).

Other factors influencing survival
Left bundle branch block (LBBB) was evident in 64 patients (73.5 ± 10.3 years) and right bundle branch block (RBBB) in 35 patients (75.8 ± 11.5 years). Mean survival time for patients with LBBB was 50.8 months, for patients with RBBB 52.2 months, for those without BBB (n = 1528; 73.9 ± 9.0 years) 86.5 months, these differences were not significant.

Regarding symptoms leading to PM therapy, 282 patients (75.2 ± 8.7 years) suffered syncope, 147 (74.1 ± 8.4 years) near-syncope, and in 1182 patients (73.5 ± 9.3 years) non-symptomatic bradycardia was the reason for PM implantation. Mean survival time was 71.6 months in those implanted after syncope and 82.5 months in those implanted after non-symptomatic bradycardia. Longest mean survival was found in those implanted for near-syncope (115.8 months, P < 0.05).

Discussion
Despite the fact that AF is a large-scale clinical problem with high and increasing incidence and prevalence rates especially in the elderly,11 available epidemiologic data on mortality are quite sparse and sometimes contradictory. Whereas data from the Framingham Study8 suggest an increased mortality in patients with AF, the more recent Veterans Administration Heart Failure Trials (V-HeFT) and the Carvedilol Or Metoprolol European Trial (COMET) did not show an increased mortality among patients with concomitant AF at study entry.12,13 Our data suggest that, at least in AF patients with PMs, mortality has substantially decreased within the last three decades with more than doubling survival times from 66.8 months in the seventies to 139.8 months in the nineties. This at least in
part explains the discrepancy outlined above, as data from the Framingham study have been collected years ago. There, mortality rates at 10-year follow-up for men (61.5%) and women (57.6%) with AF were significantly higher than those in an age- and sex-matched population. These rates are in line with our results from the seventies (10-year mortality 65.0%).

According to data provided by the Statistisches Landesamt Baden-Württemberg, the overall average life expectancy of a 75 years old man (woman) in our region has increased between 1970 and 1999 from 82.33 (83.62) to 84.88 (87.05) years. In our population, we observed an increase from 76.77 (80.01) years in the seventies to 84.95 (89.71) years in the nineties (calculated mean age at implantation + median survival). This supports our finding that the effect of AF on mortality has declined and is not solely an effect of the reduction in overall mortality within the last decades.

As expected, younger age at implantation predicts longer survival. Patients with pre-syncope lived significantly longer than those implanted for syncope or non-symptomatic bradycardia, a finding that has previously been described and attributed to selection bias: those with near-syncope may represent a ‘healthier’ collective.

It has been shown that LBBB is an independent marker of mortality. In our population, mean survival was 50.8 months in those with LBBB as compared with 86.8 months in those without conduction delay. Possibly due to the low prevalence of LBBB, this difference remained statistically insignificant.

Female gender predicted longer survival in our population (despite older age at implantation) with median survival of 7.8 years (vs. 5.9 years in men). This is in concordance with the longer overall life expectancy and the delayed appearance of cardiovascular disease in women. In contrast to our findings, in the Framingham cohort AF diminished the female advantage in survival.

Our data strongly suggest a decrease in mortality in patients with AF within the last decades, making the need for further current data on the impact of AF on the prognosis in different clinical settings obvious.

Limitations of the study
As data collection started in the 1970’s, information on AF-related co-morbid conditions such as the presence of hypertension, diabetes, coronary artery disease, heart
failure, or valve disease is—due to incomplete patient records and a not standardized cardiological work-up protocol for the included patients—sparse. The assumption that improvement in therapy of these conditions and the implementation of anticoagulation are responsible for the decrease in mortality therefore is speculative. As only PM patients were included in our study, these results should not be transferred to AF patients without PM uncritically.

Conflict of interest: none declared.

References