Medium-long-term mortality and change in functional status in elderly patients with pacemaker

Morbimortalidad cardiovascular y variación del grado funcional en pacientes ancianos portadores de marcapasos

Pedro Pérez-Díaz1*, Javier Jiménez-Díaz1, Felipe Higuera-Sobrino1, Jesús Piqueras-Flores1, Raquel Frías-García1, Virginia Mazoteras-Muñoz2, Ramón Maseda-Uriza1, and Violeta Arenas-Cambronero3

1Department of Cardiology; 2Department of Geriatrics; 3Family and Community Medical Care Teaching Unit (UDMAFYC), Hospital General Universitario de Ciudad Real, Ciudad Real, Spain

Abstract

Background: Nowadays, 49% of patients with pacemakers are older than 80 years old. Nevertheless, mortality and change in functional status after pacemaker implantation are not well documented in elderly patients. Objective: We designed a prospective study to analyze the cardiovascular mortality and change in functional status of elderly patients, medium-long term after pacemaker implantation. Methods: An observational study including pacemaker implants in individual older than 70 years old in a single-center university hospital between 2012 and 2014. Analysis testing for an association between pacemaker system, medium-long-term mortality, and functional status after implantation was undertaken. Results: About 60% of patients were older than 80 years old. The third-degree atrioventricular blockage (44.3%) and slow ventricular response atrial fibrillation (16.7%) were the most frequent electrocardiogram abnormalities, while bicameral DDD was the sort of pacing our department used the most (38.6%) (VVI in octogenarian patients, 38.7%). Long-term mortality was significantly higher in ventricular devices, especially in octogenarian patients (p = 0.001). Single-chamber VVI pacing acted as independent predictors of all-cause mortality in these individuals (p = 0.001). We found no significant improvement in Barthel Index and functional status in this subgroup of patients, 3 years after pacing. Conclusions: Long-term mortality in individuals older than 80 years old with pacemaker implantation was significantly higher comparing with general population, especially in ventricular devices. No significant improvement in functional status was detected in this subgroup of patients.


Resumen

Objetivo: Aproximadamente un 49% de los implantes se efectúan a individuos mayores de 80 años; sin embargo, la evidencia científica sobre mortalidad y cambio en la situación funcional de estos pacientes es muy pobre. Diseñamos un estudio

Correspondence:
*Pedro Pérez-Díaz
Hospital General Universitario de Ciudad Real
Servicio de cardiología (5.ª B) Calle del Obispo Rafael Torija, s/n 13005 Ciudad Real, España
E-mail: pedroperezdiaz5@gmail.com

Date of reception: 30-09-2018
Date of acceptance: 14-01-2019
Available online: 02-10-2019
Arch Cardiol Mex (Eng). 2019;89(3):212-220
DOI: 10.24875/ACME.M19000052
2604-7063/© 2019 Instituto Nacional de Cardiología Ignacio Chávez. Published by Permanyer. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
Introduction

Permanent pacemaker is the treatment of choice for significant bradyarrhythmia, usually caused by degeneration of the excitation-conduction cardiac system associated with old age. The 2013 European Society of Cardiology guidelines on cardiac pacing established symptomatic sinus node dysfunction, symptomatic second-degree Mobitz I and Mobitz II, and the third-degree atrioventricular block (AVB) as fundamental indications for permanent pacemaker implantation. The most common indications for permanent pacemaker implantation are third-degree AVB followed by symptomatic sinus node dysfunction, a trend that has remained stable over the past few years. However, due to the progressive increase in life expectancy that has taken place in Spain in recent years, mean age at pacemaker implantation has increased from 77 years in 2012 to 77.8 years in 2016. About 50% of total pacemaker implantations correspond to individuals older than 80 years. Nevertheless, most available scientific evidence is based on studies conducted with middle-aged patients below the age of the population usually served in arrhythmia units, and some of these trials even exclude this subgroup of patients.

Although the ventricular stimulation mode (VVI) is indicated in patients with atrial fibrillation and AVB, it is also used in patients with advanced AVB and high comorbidity or limited life expectancy. Physiological devices, such as AAI, VDD, and DDD, which allow a sequential pacing that maintains atrioventricular synchrony, are implanted in individuals with symptomatic sinus node dysfunction or advanced AVB. In Spain, the most widely used stimulation mode is DDD (47.2%) followed by VVI (39.3%) and, far behind, by VDD (10.2%).

At present, there is controversy about the benefits of physiological cardiac pacing in comparison with ventricular pacing in terms of morbidity and mortality. Ventricular stimulation has been associated with a higher incidence of atrial fibrillation and heart failure than physiological cardiac pacing, as demonstrated by the DANPACE and MOST trials. However, no study has shown conclusive differences with regard to mortality.

On the other hand, the results in quality of life and functional status improvement in elderly patients after pacemaker implantation are contradictory. The PASE trial demonstrated significant improvement in quality of life at 3 months post-pacemaker implantation, regardless of uni- or bicameral pacing. However, these findings have not been confirmed in other studies.

The main purpose of our study was to analyze cardiovascular and overall mortality in the mid-term in elderly patients with permanent cardiac pacing. The secondary outcomes we looked for were the description of cardiovascular events and the change in functional status after pacemaker insertion.

Materials and methods

A prospective, observational study included 308 consecutive patients older than 70 years undergoing elective permanent pacemaker implantation between January 2012 and December 2014 at the Arrhythmia Unit of the University General Hospital of Ciudad Real. The inclusion criteria were patients older than 70 years with permanent pacemaker indication according to the European Society of Cardiology current guidelines on cardiac pacing. Patients younger than 70 years, patients undergoing resynchronization or defibrillator implantation, patients with left ventricular ejection fraction (LVEF) lower than 35%, and patients undergoing generator replacement were excluded from the study.
Baseline characteristics and follow-up

We analyzed the baseline characteristics, including diabetes mellitus, dyslipidemia, hypertension, chronic obstructive pulmonary disease, atrial fibrillation, LVEF, glomerular filtration (according to the Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] formula), indications for primary implantation, and the type of pacing (ventricular, in the case of VVI, or physiological, in the case of AAI, VDD or DDD). The recorded peri-procedure complications were atrial/ventricular electrode dislocation, cardiac perforation, pneumothorax, hematoma requiring transfusion, and infection of the pacemaker system. In addition, geriatric functional assessment was performed at admission and at 3 years of the device implantation using the Barthel Functional Index over a score of 100 and the Red Cross Functional (RCF) scale. The primary outcome variable was all-cause mortality. Secondary outcome variables were post-implantation complications, cardiovascular events (defined as acute coronary syndrome, heart failure, and stroke), cardiovascular mortality, and functional and cognitive status modification at end of follow-up.

Statistical analysis

The statistical analysis was carried out with the SPSS program, version 18.0 (SPSS Inc., Chicago, Illinois). The test used to check data normal distribution was the Kolmogorov–Smirnov test. The data are expressed as the mean ± standard deviation (SD). The age at pacemaker implantation and LVEF variables did not follow a normal distribution (median 82 years – interquartile range 6 and mean 60% – interquartile range 3%, respectively); however, we used centralization and dispersion parameters for their statistical analysis, due to a coefficient of variation of < 33% and an important sample size. To compare continuous variables between both groups, we used Student’s t-test for independent samples (or Mann–Whitney U-test if there was no normal distribution). To compare more than two means, we used the ANOVA test and Tukey’s test for post hoc analysis. The Chi-square test (or Fisher’s test if a subgroup had a representation of < 5 individuals) was used to assess differences between qualitative variables. We analyzed mortality predictors through logistic regression, introducing all-cause mortality at the end of the follow-up period as a dependent variable, and cardiovascular risk factors, valvulopathies, pacing modes, heart failure, and chronic renal failure as independent variables. In addition, we carried out a survival analysis using the Kaplan–Meier method with comparative survival analysis using the log-rank test. Statistical significance was considered with p = 0.05.

Results

Baseline characteristics

Among the entire study population, the mean age at pacemaker implantation was 82.1 ± 5.1 years (52.6% of males), and it was significantly higher in the ventricular pacing group (84.4 ± 5.3 vs. 81 ± 4.7; p < 0.001). The most common indication for pacemaker implantation was complete heart block (44.3%) followed by slow or blocked atrial fibrillation (16.7%) and symptomatic second degree AVB (13.8%). Single-chamber pacemakers were implanted in 35.1% of patients, while 64.6% received a dual-chamber device. The most commonly used pacing mode was DDD (38.6%) followed by VVI (32.1%) and, very closely, by VDD (27.6%) (Tables 1 and 2).

The subgroup of octogenarian patients with pacemaker primary implantation was composed of 186 patients,
with a mean age of 85 ± 4 years (51.1% of males). The most common electrocardiographic abnormality that drove to implantation continued to be advanced AVB, while the most commonly employed device was VVI (38.7%) followed by VDD (38.2%) and by DDD (21.5%). In the octogenarians with complete heart block, VDD mode was the most widely used (56.4%) followed by VVI (25.5%) and DDD (18.1%) (Fig. 1). Of note, a proportion of tricuspid regurgitation and upper pulmonary hypertension was also observed in the VVI devices (12.5% vs. 0.9% and 15.3% vs. 3.5%, respectively). There were no significant differences in the Barthel Index score or the RCF scale before pacemaker implantation (median 95 ± 76.2; p = 0.669 and median 2 ± 4; p = 0.749, respectively).

Follow-up

Overall mortality rate in the entire sample was 21.1% (with a mean follow-up time of 3.5 years), which corresponds approximately to the double that is expected in individuals of similar age and gender in the general population, according to data from the National Institute of Statistics (overall mortality in patients with pacemaker implantation in Ciudad Real, 20-25% [mortality in individuals of similar age and gender in the general population, 9-10%]) (INEbase, mortality tables of the population of Spain by year, gender, age, and functions). Only 18 patients (5.8%) had complications during the immediate or early post-operative period, of which 10 (56%), 6 (33%) and 2 (11%) corresponded to patients undergoing DDD, VDD, and VVI pacing modes, respectively. There were no differences in the overall statistical analysis in terms of complications or cardiovascular events according to the pacing mode. Although we detected a higher rate of atrial fibrillation episodes in physiological devices, most of these episodes were detected in the pacemaker electrogram analysis and, therefore, comparisons are not valid due to the absence of atrial activity detection by VVI devices. Cardiovascular and all-cause mortality at the end of the follow-up period was higher with ventricular than with physiological

<table>
<thead>
<tr>
<th>Table 2. Comparative analysis of baseline characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Ventricular pacemaker</td>
</tr>
<tr>
<td>------------------------</td>
</tr>
<tr>
<td>Age at pacemaker implantation (years)</td>
</tr>
<tr>
<td>Gender</td>
</tr>
<tr>
<td>– Female</td>
</tr>
<tr>
<td>– Male</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
</tr>
<tr>
<td>Dyslipidemia</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td>Moderate-severe mitral stenosis</td>
</tr>
<tr>
<td>Moderate-severe mitral regurgitation</td>
</tr>
<tr>
<td>Moderate-severe aortic stenosis</td>
</tr>
<tr>
<td>Moderate-severe aortic regurgitation</td>
</tr>
<tr>
<td>Moderate-severe tricuspid regurgitation</td>
</tr>
<tr>
<td>Moderate-severe pulmonary hypertension</td>
</tr>
<tr>
<td>Paroxysmal/persistent atrial fibrillation</td>
</tr>
<tr>
<td>Permanent (chronic) atrial fibrillation</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
</tr>
<tr>
<td>Chronic heart failure</td>
</tr>
<tr>
<td>Moderate-severe CKD (GFR ≤ 45 mL/min)</td>
</tr>
</tbody>
</table>
devices (33.3 vs. 15.3%; odds ratio [OR]: 0.4; 95% confidence interval [CI]: 0.2-0.6; p < 0.001) (Table 3).

In octogenarian individuals, we did not detect significant differences in the rate of post-implantation complications, atrial fibrillation, acute coronary syndrome, or heart failure (4.2 vs. 8.6%; OR: 2.2; 95% CI: 0.2-19; p = 0.674; 0 vs. 7.1%; OR: 0.7; 95% CI: 0.6-0.8; p = 0.324; 4.2 vs. 1.4%; OR 0.3; 95% CI: 0.02-5.5; p = 0.249, and 20.8 vs. 12.9%; OR: 0.6; 95% CI: 0.2-1.9; p = 0.415, respectively). However, the rate of all-cause mortality at 2 and 3 years and at end of the follow-up period was higher with ventricular versus physiological devices (50 vs. 14.3%; OR: 0.2; 95% CI: 0.06-0.5; p = 0.001; 63.6 vs. 20%; OR: 0.1; 95% CI: 0.04-0.6; p = 0.007, and 54.2 vs. 18.6%; OR: 0.2; 95% CI: 0.07-0.5; p = 0.001, respectively). These results were maintained when patients with severe valvulopathies were excluded since the start of the analysis. In the octogenarian patients with advanced AVB, the results were similar: we did not detect any significant difference in the rate of readmissions for acute coronary syndrome (p = 0.249) and heart failure (p = 0.415) in association with the stimulation mode (VVI vs. VDD vs. DDD), although we found higher overall mortality at 2 years post-implantation (p = 0.001), 3 years post-implantation (p = 0.004), and at the end of the follow-up period (p = 0.001) with ventricular devices with regard to the VDD and DDD devices (Fig. 2).

An age-adjusted subgroup analysis, where we compared individuals with advanced block and pacing with VVI mode with those who received VDD pacing, did not show significant differences in the rate of readmissions for heart failure or cardiovascular events, although, as in the overall analysis, patients showed higher overall mortality at the end of the follow-up period.

The multivariate analysis defined chronic heart failure and VVI pacemaker as independent mortality predictors in octogenarian patients with pacemaker indication (p = 0.034, p = 0.024, and p = 0.001, respectively). Median time to all-cause death was 0.9 years, with no differences between ventricular (1.01 ± 0.5 years [median ± interquartile range]) and physiological pacing modes (0.9 ± 1.6 years [median ± interquartile range]) (p = 0.608).

In addition, we carried out an age-adjusted sub-analysis excluding those patients with serious valvulopathies to study the rate of hospitalizations for heart failure and long-term cardiovascular and overall mortality. This
Table 3. Overall cardiovascular morbidity and mortality

<table>
<thead>
<tr>
<th></th>
<th>Ventricular pacemaker</th>
<th>Physiological pacemaker</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-year all-cause mortality</td>
<td>16 (16.2%)</td>
<td>13 (6.2%)</td>
<td>0.344 (0.158-0.747)</td>
<td>0.005</td>
</tr>
<tr>
<td>1-year cardiovascular mortality</td>
<td>5 (5.1%)</td>
<td>6 (2.9%)</td>
<td>0.556 (0.165-1.867)</td>
<td>0.326</td>
</tr>
<tr>
<td>2-year all-cause mortality</td>
<td>28 (28.3%)</td>
<td>23 (11%)</td>
<td>0.314 (0.169-0.580)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>2-year cardiovascular mortality</td>
<td>9 (9.1%)</td>
<td>6 (2.9%)</td>
<td>0.296 (0.102-0.855)</td>
<td>0.018</td>
</tr>
<tr>
<td>3-year all-cause mortality</td>
<td>6 (13%)</td>
<td>5 (3.7%)</td>
<td>0.447 (0.209-0.954)</td>
<td>0.025</td>
</tr>
<tr>
<td>3-year cardiovascular mortality</td>
<td>6 (13%)</td>
<td>5 (3.7%)</td>
<td>0.256 (0.074-0.885)</td>
<td>0.022</td>
</tr>
<tr>
<td>End of follow-up all-cause mortality</td>
<td>33 (33.3%)</td>
<td>32 (15.3%)</td>
<td>0.362 (0.206-0.635)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>End of follow-up cardiovascular mortality</td>
<td>11 (11.1%)</td>
<td>8 (3.8%)</td>
<td>0.318 (0.124-0.819)</td>
<td>0.032</td>
</tr>
<tr>
<td>Post-pacemaker implantation complications</td>
<td>2 (2%)</td>
<td>15 (7.2%)</td>
<td>4.021 (0.906-17.842)</td>
<td>0.140</td>
</tr>
<tr>
<td>Atrial fibrillation “de novo” episodes</td>
<td>0 (0%)</td>
<td>17 (8.1%)</td>
<td>0.660 (0.608-0.717)</td>
<td>0.004</td>
</tr>
<tr>
<td>Acute coronary syndrome</td>
<td>1 (1%)</td>
<td>3 (1.4%)</td>
<td>1.413 (0.145-13.756)</td>
<td>0.765</td>
</tr>
<tr>
<td>Acute heart failure</td>
<td>21 (21.2%)</td>
<td>25 (12%)</td>
<td>0.507 (0.288-0.960)</td>
<td>0.025</td>
</tr>
<tr>
<td>Stroke</td>
<td>6 (6.1%)</td>
<td>6 (2.9%)</td>
<td>0.458 (0.144-1.458)</td>
<td>0.177</td>
</tr>
</tbody>
</table>

Figure 2. Cardiovascular and all-cause mortality in octogenarian patients with primary pacemaker implantation. 

As for the relationship of cardiac pacing with functional status modification, we analyzed 82 elderly patients in whom we were able to quantify their Barthel substudy revealed differences in the latter parameter in favor of patients with physiological versus ventricular pacing, as it was observed in the overall analysis.
We did not detect significant differences in the variation on the Barthel Index and RCF scale in octogenarian patients with sinus node dysfunction, second-degree symptomatic AVB, intraventricular conduction disorder, and atrial fibrillation. In fact, individuals older than 80 years with complete heart block had a mean variation in the Barthel Index of $-17.7 \pm 27.1$ ($p < 0.001$) and a mean variation in the RCF scale of $0.9 \pm 1.3$ ($p < 0.001$) (Fig. 3).

Discussion

The progressive increase in age at pacemaker implantation entails an increase in comorbidity, morbidity, and mortality, a finding that we have confirmed with the presented results. Mean age in most observational and experimental studies related to permanent cardiac pacing does not exceed 78 years, and in almost all these trials, the subgroup of octogenarian patients is absolutely underrepresented. However, in our sample, the mean age was higher and probably better reflects the real situation of pacemaker implantation at present.

The difference in the rate of VDD pacemaker utilization between our study population and the general population can be explained by the exclusion of individuals younger than 70 years and the tendency toward trying to maintain atrioventricular synchrony in elderly patients with high comorbidity and advanced block in our unit.

There is controversy on whether the VDD mode offers advantages over VVI in this context with regard to the preservation of atrioventricular synchrony. Some studies suggest a certain benefit with the use of the VDD pacing mode in patients with a preserved sinus node function and AVB, although there is an increased risk of atrial sensing loss overtime. On the other hand, there are no clear morbidity and mortality differences either between VDD and DDD. In our study, we did not detect differences in the rate of post-implantation complications or cardiovascular events (acute coronary syndrome and/or hospitalization for heart failure) in octogenarian individuals with advanced block dependent on the pacing mode (VVI, VDD, and DDD) ($n = 94$), although we observed a higher mortality rate in the mid-long-term with ventricular versus physiological devices. The multivariate analysis defined the VVI pacing mode as an independent mortality predictor in this...
subgroup of patients. The limitation that entails having a relatively small sample size of octogenarian patients with complete heart block (94) forces us to be cautious for drawing firm conclusions, although this allows us formulating the hypothesis that the VDD pacemaker can be a valid and useful alternative in elderly patients with pacemaker indication for advanced block and high comorbidity.

In our analysis, we did not detect a significant improvement in the functional or cognitive status of patients in the mid-long term, and even in some patients, such as patients with advanced block, functional status was significantly poorer after the pacemaker implantation. We suggest that, in old and very old patients, actions should be guided within the field of bradycardiac rhythms depending on what the cardiac pacing guidelines indicate. However, probably, we should consider other variables such as the probability of modifying the degree of both physical and psychological dependence. Perhaps, a mean of 3.5 years of follow-up is too long for the analysis of this functional degree in a sample with such an elevated mean age. This could partly explain such discouraging results in this context and would be the basis for future prospective studies, with shorter follow-up periods (1 month, 6 months, 1 year, etc.). In view of these findings, we must be cautious in octogenarian patients and not give false expectations since finding a significant improvement in functional and cognitive ability does not seem foreseeable, at least in the medium term. We must assume that functional impairment will depend on other factors, and not only on intrinsic properties of the cardiac excitation-conduction system.

Limitations

The ventricular device implantation indication (beyond slow or blocked atrial fibrillation) was established by the operator in question based on patient comorbidity and risk of complications, but in the absence of objective parameters that quantified both, which can induce selection bias. In addition, mean age at pacemaker implantation was significantly higher for ventricular than for physiological devices, which can introduce important artifacts in the morbidity and mortality results, especially considering that we are dealing with a population with important comorbidities. Finally, the relative sample size that we obtained when analyzing octogenarian patients with block (n = 94) and those in whom we could perform previous and post-pacemaker implantation geriatric assessment (n = 82) (of the initial sample of 308 and 186 octogenarians), does not allow us drawing firm conclusions, but to formulate new hypotheses that should be corroborated in future studies.

Conclusions

Cardiovascular morbidity and mortality in patients older than 80 years who are pacemaker carriers are high and far superior to that of the general population of equal age. With the results of our study, the use of dual-chamber devices, such as VDD, could be considered to guarantee a certain degree of atrioventricular synchrony in octogenarian patients with persistent AVB and preserved sinus node function, without thereby increasing cardiovascular morbidity and mortality.

Long-term improvement of physical or cognitive functional status is non-existent, just as we have demonstrated. So much so that there are even subgroups of patients in whom this parameter is significantly worse 3 years after implantation. In our working group's opinion, we believe that prospective studies are needed where short-term functional status variation is analyzed in the elderly and very elderly patients (comparing, for example, the Barthel Index immediately before the implantation, with the score recorded 1 month, 3 months, or 6 months post-implantation) since the elevated half-life of our patients (with their consequent comorbidities and limitations) can introduce artifacts in long-term results.

Conflicts of interest

None.

Funding

No funding.

Ethical disclosures

Protection of people and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained written informed consent of the patients and/or subjects mentioned in the article. The corresponding author is in possession of this document.


