

# Poor Health-Related Quality of Life of Patients with Indication for Chronic Cardiac Pacemaker Therapy

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**Background:** Studies on health-related quality of life (HRQoL) of patients awaiting pacemaker (PM) implantation are scarce, or executed in specific patient subgroups (regarding age or specific cardiac rhythm disorders). The purpose of this study was to systematically assess the HRQoL in a large unselected cohort of patients with a conventional indication for PM therapy.

**Methods:** Pre-PM implantation HRQoL (measured with the SF-36 questionnaire, completed at hospital admission) of 818 consecutive Dutch patients included in the FOLLOWPACE study was compared with the HRQoL in a sample of the general Dutch population, and with several cohorts of patients with other conditions. Linear regression analysis was performed to analyze determinants of this HRQoL.

**Results:** Almost all SF-36 subscale scores were substantially and significantly lower in the PM patients compared to the general population, with  $P$ -values  $< 0.001$  in all SF-36 subscales except for “pain” and “general health perception.” In the PM patients, presence of comorbidities, gender, and age were significantly associated with the overall physical component summary score (mean  $38.8 \pm 27$  standard deviation) whereas the overall mental component summary score ( $46.8 \pm 27.0$ ) was associated with gender and age.

**Conclusion:** The HRQoL of patients before first PM implantation is significantly lower than that of a general population and also various other patient populations. Physicians should be aware of this unfavorable condition and keep the time interval between the diagnosis of a cardiac rhythm disorder requiring PM implantation and the implantation procedure as short as possible. (PACE 2008; 31:480–486)

## pacemaker, rhythm disorders, quality of life, SF-36, comparison, determinants

### Introduction

Since the early 1980s health-related quality of life (HRQoL) has evolved to a well-known validated and widely used tool to assess outcomes of medical therapies, including pacemaker (PM) therapy.<sup>1–6</sup> Methods to summarize the answers or results of all these questionnaires and how to reflect their clinical relevance have also been reported.<sup>2,5,7–11</sup> The HRQoL of patients with cardiac rhythm disorders requiring the implantation of a PM or already having a PM has been reported

in previous studies.<sup>12–19</sup> These studies, however, applied a nonvalidated questionnaire to measure HRQoL, were based on a small sample size, or most importantly studied a specific patient subgroup such as elderly patients or patients with specific cardiac rhythm disorders,<sup>12–15</sup> whereas some studies only addressed the improvement of HRQoL after PM implantation.<sup>14–17,19</sup> Furthermore, previous published data on factors influencing HRQoL of patients awaiting a first PM implantation are inconclusive and comparisons of this HRQoL with a general population and patient groups with various other diseases have never been published.

The purpose of this report of the Dutch multicenter prospective FOLLOWPACE study, which includes patients with conventional reasons for chronic pacing,<sup>20</sup> was to assess determinants (such as patient's gender, age, Body Mass Index (BMI), cardiac history, and pacing indication) of HRQoL and to compare the baseline health perception (before PM implantation) in an unselected population of patients awaiting PM implantation with a general population and other patient cohorts.<sup>21</sup>

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## Methods

### Patients

This article describes the information retrieved from a cohort of 818 patients included between January 2004 and January 2007, in a multicenter prospective longitudinal cohort study, executed in 24 (of the 104) PM centers in The Netherlands, the FOLLOWPACE study. The design of the FOLLOWPACE study has been published previously.<sup>21</sup> In brief, FOLLOWPACE was designed as a prospective cohort study to systematically document the PM implantation procedure as well as the routine follow-up in patients with cardiac rhythm disorders in The Netherlands. No specific recommendations on methods of therapy or follow-up were provided to the study centers. FOLLOWPACE was purely designed as an observational—not an interventional—study in an unselected population.

FOLLOWPACE included all consecutive patients (during the study period in the participating hospitals) aged 18 years and over, hospitalized for the implantation of a PM for conventional reasons, including atrioventricular conduction disturbances, sick sinus syndrome, bradytachycardias, and atrial fibrillation with a slow ventricular response.<sup>20</sup> The purpose was to gather information of an unselected patient population leading to general applicability of the study results, and reflecting daily practice. Patients awaiting their first PM implantation in one of the 24 participating centers were potential candidates for this study. Patients were not eligible if they declined to participate or were participating in another clinical trial. In addition, patients having diseases that were likely to cause death or significant morbidity during the study period such as carcinoma and immune, infectious or degenerative diseases influencing cognitive functions were excluded. At hospital admission just before PM implantation, patients were asked to fill out various HRQoL questionnaires, that is, the general SF-36 and EQ5D questionnaires,<sup>22,23</sup> and the disease specific AquaRel questionnaire.<sup>24</sup> The protocol for this study was approved by the Ethical Commission of the University Medical Center (UMC), Utrecht, The Netherlands. The FOLLOWPACE study adhered to the tenets described in the Declaration of Helsinki.

### Health-Related Quality of Life

The HRQoL of this cohort and in all other comparison groups was measured by the SF-36. The Medical Outcomes Study Short-Form Health Survey<sup>6,23,25–27</sup> (SF-36) is the most widely used generic questionnaire because of its psychometric characteristics and ability to compare HRQoL across different patient categories. This questionnaire consists of 36 questions, which can be com-

prised of eight subscales that measure: (1) physical functioning (PF); (2) role limitations due to physical problems (RP); (3) social functioning (SF); (4) role limitation due to emotional problems (RE); (5) mental health (MH); (6) bodily pain (BP); (7) sense of vitality (EV), and (8) general health (GH). Furthermore, the SF-36 can further be comprised into two overall scores: a physical component scale (PCS) and a mental component subscale (MCS).<sup>27</sup> Scores of each (sub)scale are normalized to a scale ranging from 0 to 100, with a lower score representing a lower HRQoL.

### Comparison Groups

We compared the HRQoL of our patients awaiting PM implantation with an (as much as possible age-matched) sample from the general Dutch population and various other patient samples. Data on the HRQoL (measured with the SF-36 questionnaire) of a sample of the general Dutch population, were obtained from a previous study by VanderZee.<sup>28</sup> In addition, we selected papers from multicenter studies published after 1992 and with more than 100 included patients, with full data on SF-36 scores. We selected seven different patient cohorts: patients with hypertrophic cardiomyopathy,<sup>29</sup> diabetes,<sup>30</sup> rheumatoid arthritis (RA),<sup>31</sup> chronic angina pectoris (cAP),<sup>32</sup> migraine,<sup>33</sup> epilepsy,<sup>30</sup> and patients included in a cardiac rehabilitation program<sup>34</sup> before any intervention was performed.

### Data Analysis

For our patients in the FOLLOWPACE study, we first established whether the values of SF-36 scores were normally distributed using visual inspection to detect skewness of the data and the Shapiro-Wilk *W*-test, which tests the hypothesis that there is a correlation between the observed values and the normal scores. When the hypothesis is rejected, the distribution is considered as being normal. We assumed a normal distribution for the HRQoL data in the comparison groups where only means and standard deviation were provided. Next we computed the mean differences for all SF-36 subscales between our cohort of PM patients and the general population, and patients with other diseases. Statistical significance of these mean differences was tested using the Student's *t*-test.

Several studies have been published on the interpretation and clinical relevance of statistically significant differences in mean scores of SF-36 subscales.<sup>7,35–39</sup> To appreciate mean differences of SF-36 data, Cohen introduced the measurement and interpretation of the so-called effect size for HRQoL. An effect size can be computed by dividing the mean difference of the score in each SF-36 subscale between a patient group and a control

group by the standard deviation of the mean of the control group. An effect size of  $<0.20$  can be considered as clinically irrelevant,  $0.20$ – $0.49$  as small,  $0.50$ – $0.79$  as moderate, and an effect size of  $>0.80$  as large and highly relevant.<sup>40</sup>

Finally, a multivariable linear regression analysis was performed on both the overall PCS and MCS scores of the SF-36 to determine whether the patient's gender, age, Body Mass Index (BMI), cardiac history, and pacing indication were independently related to the HRQoL. All analyses were performed using S-Plus Version 6.2.1 (Insightful Corp., Seattle, WA, USA).

### Results

The baseline characteristics of our 818 PM patients are given in Table I. Age distribution and indications for pacing were concordant with that in the rest of Europe,<sup>41</sup> with a mean age of 73.2 ( $\pm 10.5$ ) years and atrioventricular conduction disturbances as the most frequent primary indication for PM implantation.

Patients awaiting PM implantation had a significantly lower HRQoL than the general population with a comparable age distribution ( $P < 0.001$ ), for all SF-36 scales except for the subscales "BP" ( $P = 0.16$ ) and "GH" ( $P = 0.17$ ). (Table II)

**Table I.**

Baseline Characteristics of 818 Patients Awaiting First PM Implantation

Patient Characteristics	
Male	60.6
Age in years (range 22–99)	73.2 (10.5)
Age categories	
22–60 (n = 103)	12.6
61–70 (n = 171)	20.9
71–80 (n = 347)	42.4
81–100 (n = 197)	24.1
Cardiac history (Prior AMI and/or PTCA/ CABG, heart failure, other*)	67.5
Main indication for implantation	
Atrioventricular conduction disturbances (n = 340)	41.5
Sick sinus syndrome, bradycardias (n = 278)	34.0
Atrial fibrillation with slow ventricular response (n = 141)	17.2
Heart failure (n = 22)	2.7
Other (n = 37)	4.5

Numbers are percentages unless stated otherwise.

Abbreviations: AMI = acute myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty; CABG = coronary arterial bypass graft.

\*Peripheral vascular disease, His ablations.

The largest difference regarded the subscale "RP" where the observed difference was 38.3 (95% CI: 30.4–46.1) with an effect size of 0.96. The differences in the two overall scores (PCS:  $38.8 \pm 27.1$  vs  $43.7 \pm 28.5$  and MCS  $46.8 \pm 27.0$  vs  $53.2 \pm 24.1$ ) were somewhat smaller with P-values of 0.08 and 0.02, and effect sizes of 0.18 and 0.24, respectively (Table II).

The PM population was older (mean 73.2  $\pm$  10.5 years) than the patients in the cardiac rehabilitation study ( $59.7 \pm 11.0$  years), and the patients with hypertrophic cardiomyopathy ( $43.2 \pm 14.7$  years). The values of all SF-36 scales in these cohorts were similar, except for the latter patient group on the subscale "RP" (Table III). Patients with cAP were younger than the PM patients ( $67.0 \pm 10.0$  years vs  $73.2 \pm 10.5$  years), but scored higher on the subscales "PF" and "RP" (effect sizes of 0.86 and 0.59, respectively) and lower on the "MH" subscale (effect size 0.50). Patients with diabetes scored a higher HRQoL score for the scales "PF," "SF," and "RP," (effect sizes: 0.77, 0.55, and 0.61). Patients with migraine scored higher on the subscales "PF," "RP," "RE," and "GH" (effect sizes of 1.32; 0.63; 0.62, and 0.76) and lower on "BP" (effect size 0.80). Patients with RA scored similar to patients awaiting PM implantation on most SF-36 subscales but lower on "EV" and "BP" (effect sizes 0.56 and 1.26). Patients with epilepsy scored higher on "PF," "RP," and "GH" (effect sizes 0.95, 0.73, and 0.59).

Multivariable linear regression modeling identified patients' gender, presence of heart failure, and diabetes, higher age, and Body Mass Index as independently associated with lower scores on the overall PCS score (Table IV). Gender and age were independently associated with the overall MCS score, where MCS was lower in female and younger patients.

### Discussion

To appreciate our findings, several aspects of the study need consideration. First, when comparing HRQoL between a general population and different patient populations, a non-disease-specific HRQoL questionnaire should be used. The disadvantage of such a questionnaire, however, is the lack of sufficient specificity to detect disease-specific impairment of health perception in the comparison between different patient groups, potentially undermining the comparability. To reduce this potential we carefully selected data on several patient cohorts that were published not too long ago and obtained from relatively large studies ( $N > 100$ ). Obviously, differences between the patient populations can still exist. Unfortunately, the papers describing these other patient groups did not present sufficient baseline data to allow

**Table II.**

Mean Scores (SD) of the SF-36 Subscales of Patients Awaiting First PM Implantation (n = 818) in Comparison with an Approximate Age Matched Average Dutch Population (65–75 years, n = 118)

	<b>Patients Awaiting PM Implantation (n = 818)</b>	<b>Average controls (65–75 years) (n = 118)</b>	<b>Difference (95%CI)</b>	<b>Effect size*</b>	<b>P-Value</b>
Physical functioning	53.6 (28.7)	66.7 (26.0)	13.2 (8.0–18.3)	0.49	<0.001
Social functioning	66.0 (27.9)	83.2 (23.7)	17.2 (11.9–22.5)	0.62 <sup>†</sup>	<0.001
Role limitation (physical)	30.8 (40.0)	69.1 (42.5)	38.3 (30.4–46.1)	0.96 <sup>‡</sup>	<0.001
Role limitation (emotional)	53.8 (44.8)	82.9 (33.8)	29.1 (20.6–37.6)	0.65 <sup>†</sup>	<0.001
Mental health	69.0 (20.1)	75.9 (17.3)	6.9 (3.1–10.8)	0.34	<0.001
Energy vitality	50.9 (22.1)	64.2 (22.0)	13.3 (9.0–17.6)	0.60 <sup>†</sup>	<0.001
Pain	71.1 (26.6)	74.8 (28.0)	3.7 (–1.5–9.0)	0.14	0.16
General health perception	56.9 (20.1)	60.1 (23.9)	3.2 (–0.8–7.2)	0.16	0.17
Physical component scale	38.8 (27.1)	43.7 (28.5)	4.9 (–0.4–10.2)	0.18	0.08
Mental component scale	46.8 (27.0)	53.2 (24.1)	6.4 (1.2–11.6)	0.24	0.02

\*Cohen's effect sizes, defined as mean difference divided by the SD of the control group; (0.00–0.19) = No effect; (0.20–0.49) = Small effect; (0.50–0.79) <sup>†</sup> = Moderate effect; (>0.79) <sup>‡</sup> = Large effect.

appropriate adjustment for gender or other sociodemographic variables. Age matching could only be done for the comparison with the general population. The differences measured between our cohort and age-matched populations in the age groups 45–55 years, 55–65 years, and 65–75 years were all concordant with the differences between our total patient cohort and the comparison group at an approximate level. As the sample sizes of the age-matched population groups were fairly small, age-stratified data are not shown. Our patients had a wide age range (22–99 years) though a mean of 73.2 with standard deviation of 10.5 years. Hence, we compared the HRQoL from our PM patients with the general Dutch population with age range of 65 to 75 years.

Second, the HRQoL scores in the studies with patients with epilepsy and diabetes were adjusted for socioeconomic characteristics and comorbidity, which may have led to generally higher SF-36 scores compared to our PM population. Unfortunately, no none-adjusted data were available for these two patient groups. Also, the overall PCS and MCS were missing from almost all papers describing the other patient populations. Hence, we could only compare the difference in HRQoL on the different subscales.

Third, to improve the clinical relevance of the comparisons between our PM patients and various reference or other patient samples, we used the Cohen's effect size.<sup>40</sup> Although frequently used, this measure is dependent on the reference sample and requires some cut-off values to enhance interpretation.

Fourth, the HRQoL does not depend so much on having a particular disease, but rather on various patient characteristics, such as age, gender, comorbidities (as also reflected in the present study), and the length of the time patients suffer from the disease. From our PM population we only had cardiovascular comorbidity data, which was present in 67.5% (Table I). This may have resulted in an underestimation of differences between our study cohort and comparison patient groups with cardiac comorbidities. However, for most comparison groups information on comorbidities was not provided. Unfortunately for our PM population, the time period between the diagnosis of the cardiac rhythm disorder and the PM implantation was unknown and could therefore not be analyzed on its association with HRQoL. Furthermore, the multiple comparisons between our PM patients and the other patient groups may have produced some spuriously significant findings. To further avoid spurious significant findings, predictors of the HRQoL were only analyzed for the PCS and MCS and not for all subscales as these overall scores are a direct derivative of the subscales and closely correlated to these subscales.

Finally, to address our concerns whether the HRQoL in a general population in The Netherlands is similar to that in other Western countries<sup>42</sup> and to study whether the HRQoL in our studied cohort of patients awaiting their first PM implantation was more or less similar to that in earlier published results on HRQoL of patients awaiting PM implantation,<sup>43–45</sup> we analyzed mean differences between these groups. No major discrepancies were found

**Table III.**

Mean Scores with Standard Deviation between Parentheses of the SF-36 Scales of the Pacemaker Patients (Second Column), and the Mean Difference (with Cohen's Effect Size Between Parentheses) Per SF-36 Scale When Compared with the HRQoL of Seven Other Patient Groups

Population	Pacemaker Patients, Pre-Implantation	Cardiac Rehabilitation (Jette et al. <sup>34</sup> )	Hypertrophic Cardiomyopathy (Cox et al. <sup>29</sup> )	Angina Pectoris (Marquis et al. <sup>32</sup> )	Diabetes (Hermann et al. <sup>30</sup> )	Migraine (Jhingran et al. <sup>33</sup> )	Rheumatoid Arthritis (Kosinski et al. <sup>31</sup> )	Epilepsy (Hermann et al. <sup>30</sup> )
Mean age (SD)	73.2 (10.5)	59.7 (11.0)	43.2 (14.7)	67.0 (10.0)	58.9 (unknown)	34.2 (10.2)	63.2 (10.1)	36.3 (unknown)
N	818	789	137	170	555	303	693	271
Physical functioning	53.6 (28.7)	8.8 <sup>3</sup> (0.33)	7.4 <sup>2</sup> (0.28)	22.9 <sup>3</sup> (0.86) <sup>†</sup>	20.7 <sup>3</sup> (0.77) <sup>*</sup>	35.4 <sup>3</sup> (1.32) <sup>†</sup>	-11.6 <sup>3</sup> (0.43)	25.4 <sup>3</sup> (0.95) <sup>†</sup>
Social functioning	66.0 (27.9)	2.9 <sup>1</sup> (0.10)	4.2 (0.15)	2.6 (0.09)	15.2 <sup>3</sup> (0.55) <sup>*</sup>	8.4 <sup>3</sup> (0.30)	-1.2 (0.04)	11.3 <sup>3</sup> (0.41)
Role limitation (physical)	30.8 (40.0)	-4.2 <sup>1</sup> (0.11)	25.1 <sup>3</sup> (0.63) <sup>*</sup>	23.8 <sup>3</sup> (0.59) <sup>*</sup>	24.3 <sup>3</sup> (0.61) <sup>*</sup>	25.2 <sup>3</sup> (0.63) <sup>*</sup>	-2.7 (0.07)	29.2 <sup>3</sup> (0.73) <sup>*</sup>
Role limitation (emotional)	53.8 (44.8)	0.6 (0.01)	10.4 <sup>2</sup> (0.23)	4.1 (0.09)	16.4 <sup>3</sup> (0.37)	37.7 <sup>3</sup> (0.62) <sup>*</sup>	3.5 (0.08)	12.5 <sup>3</sup> (0.28)
Mental health	69.0 (20.1)	0.2 (0.01)	-3.4 <sup>1</sup> (0.17)	-10.2 <sup>3</sup> (0.50) <sup>*</sup>	4.0 <sup>3</sup> (0.20)	4.8 <sup>3</sup> (0.24)	1.9 (0.10)	-0.6 (0.03)
Vitality	50.9 (22.1)	-0.01 (0.001)	-7.3 <sup>2</sup> (0.33)	-2.3 (0.10)	3.4 <sup>3</sup> (0.15)	6.5 <sup>3</sup> (0.29)	-12.3 <sup>3</sup> (0.56) <sup>*</sup>	4.5 <sup>2</sup> (0.20)
Pain	71.1 (26.6)	-0.26 (0.01)	-5.0 <sup>1</sup> (0.19)	-8.0 <sup>2</sup> (0.30)	0.6 (0.02)	-21.3 <sup>3</sup> (0.80) <sup>†</sup>	-33.6 <sup>3</sup> (1.26) <sup>†</sup>	1.7 (0.07)
General health	56.9 (20.1)	3.3 <sup>2</sup> (0.16)	-9.7 <sup>3</sup> (0.48)	-5.6 <sup>2</sup> (0.28)	-4.3 <sup>2</sup> (0.21)	15.2 <sup>3</sup> (0.76) <sup>*</sup>	-1.7 (0.09)	11.8 <sup>3</sup> (0.59) <sup>*</sup>

A positive mean difference indicates that for this SF-36 scale patients with the other disease score better (higher HRQoL) than the PM patients. Cohen's Effect sizes: (0.00-0.19) = no effect; (0.20-0.49) = small effect; (0.50-0.79) = moderate effect; (>0.79) = large effect.  
<sup>1</sup>P-value<0.05, <sup>2</sup> P-value<0.01, <sup>3</sup>P-value<0.001.

**Table IV.**

Factors Independently Associated (Based on Multivariable Linear Regression Analysis) with the Overall Physical (38.8 ± 27.1) and Mental (46.8 ± 27.0) Component SF-36 Scale in 818 Patients Awaiting First PM Implantation

	B (95% CI)	P-Value
Physical component subscale (PCS)		
Female gender	-1.97 (-3.41;-0.53)	0.007
Age (in years)	-0.27 (-0.33;-0.20) <sup>*</sup>	<0.001
BMI (per unit)	-0.28 (-0.48;-0.08) <sup>*</sup>	0.006
Presence heart failure	-3.20 (-5.53;-0.87)	0.007
Presence of diabetes	-2.22 (-4.21;-0.24)	0.028
$R^2 = 0.11$		
Mental component subscale (MCS)		
Female gender	-5.80 (-7.60;-4.00)	<0.001
Age (in years)	0.14 (0.05; 0.22) <sup>*</sup>	0.001
$R^2 = 0.06$		

B and 95 % confidence intervals on patient-related factors with influence on HRQoL SF-36 physical and emotional component subscales.

Abbreviation: BMI = body mass index.

<sup>\*</sup> Per unit increase.

(results not shown). This strengthens the general applicability of the findings of our study.

**Previous Studies**

In comparison to the published data on HRQoL in patients awaiting PM implantation, our results deviate with that of Lopez et al. (PASE study)<sup>18</sup> and Fleishman et al. (MOST study),<sup>14</sup> as male patients in our cohort score generally higher on their HRQoL. Furthermore, our findings contradict with the MOST study as the HRQoL is related to the patients' comorbidity such as heart failure and diabetes. However, we confirm the results of Newman et al. (CTOPP study)<sup>19</sup> that patients at lower age tend to score higher on the physical component subscale than patients over 75 years.<sup>14,19</sup> In an unselected population of patients awaiting PM implantation both patients at younger age and of male gender tend to score higher on the MCS.

**Conclusion**

The HRQoL measured with the SF-36 questionnaire of an unselected patient population just before first PM implantation is significantly lower than that of a general population. The scales "physical functioning," "role limitation due to physical functioning," "social functioning," and "role limitations due to emotional problems" in patients awaiting a PM implantation are scored similar to that in patients joining a cardiac rehabilitation

program and to patients with rheumatoid arthritis whereas these scores are lower compared to patients with chronic angina pectoris. Several characteristics such as patients' gender, age, and the presence of cardiovascular comorbidities can support the identification of the patient with outspoken reduced quality of life before PM implantation. Awareness of these physical and emotional aspects of waiting pacemaker recipients should be translated into minimizing the time period between the diagnosis of the cardiac rhythm disorder requiring PM implantation and the implantation procedure itself, and physician's compassion with the individual patient need in terms of support and information.

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