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Original article

Factors related to the physical activity of patients with permanent cardiac pacemaker

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Abstract

Background: Over 1.3 million patients worldwide have permanent cardiac pacemakers (PPMs). In the first to third months after implantation, patients with PPM still report problems with physical activity (PA), such as limitations in their lives, jobs, and exercise; inability to perform activities as before; and decreased PA.
Objective: This study aimed to investigate the PA of patients with PPMs and identify PA-related factors (age, perceived self-efficacy, perceived benefits, perceived barriers, social support, and health literacy) in patients with PPMs.
Methods: This descriptive correlational study included 110 male and female patients with PPMs from three tertiary hospitals in Bangkok, Thailand, and was conducted using a multistage sampling technique. Data analyses involved descriptive statistics, Pearson's product–moment correlation, and Spearman's rank-order correlation.
Results: The average PA score of patients with PPMs was 6.8 (SD = 2.3). Perceived self-efficacy ($r = 0.448$, $P = 0.01$), perceived benefit (*Spearman's rho* = 0.339, $P = 0.01$), social support (*Spearman's rho* = 0.217, $P = 0.05$), and health literacy (*Spearman's rho* = 0.459, $P = 0.01$) positively related to the PA of patients with PPMs. Age and perceived barriers negatively related to the PA of patients with PPMs (*Spearman's rho* = - 0.467 and - 0.312, $P = 0.01$).
Conclusion: Nurses should encourage patients with PPMs to achieve better-perceived self-efficacy, perceived benefits, social support, and health literacy to increase their PA. Older patients with PPMs and those with negatively perceived barriers should be motivated to increase their PA levels.

Keywords: Permanent cardiac pacemaker, physical activity, related factors.

A permanent cardiac pacemaker (PPM) is a life-saving treatment for patients with very slow irregular heartbeats and helps the heart return to near-normal functions, improving patients' survival and quality of life.[1, 2] Over 1.3 million patients have PPMs worldwide,[3] and this figure is growing across all age groups. Physical activity (PA) refers to any bodily movement that requires energy expenditure in everyday living, such as work, household, transportation, sports, exercises, and hobbies.[4] According to Pender's conceptual framework, PA is a health-promotion behavior that motivates people to engage in healthy lifestyles.[5]

Owing to PA limitations different from those of other patients, patients with PPMs might experience difficulties in their everyday lives 1 - 3 months after implantation. For example, patients should avoid moving, spreading, or lying on the implanted arm for days 1 - 3. After day 3, they avoid fast and wide swinging of arms and lifting weights > 5 kg. After 3 months, they could engage in ordinary PA; however, they should avoid sports or exercises that might injure the implanted chest, such as football, basketball, volleyball, boxing, and taekwondo. These activities may cause tissue damage at the implant site, malfunctioning of the device, device displacement, or fractures.[6] Thus, patients with PPMs should engage in PA with appropriate intensity.[7]

According to a literature review, patients with PPMs report PA-related problems within 3 months after implantation. Most patients with PPMs experience limitations in their lives, jobs, and

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exercises,[8] cannot perform usual activities,[9, 10] and have decreased PA,[11] with minimal exercise (34.0%) or no exercise (44.4%).[12] PA restriction in patients with PPMs is caused by various factors, including physical, emotional, social, and environmental problems and effects on daily living after PPM implantation. For example, a patient's heart rate is unrelated to the device's function. In addition, post-procedure symptoms such as palpitations, dizziness, fainting, exhaustion, weakness, fatigue, and chest discomfort limit patients' everyday activities.[12, 13] They might also feel worthless,[11] worry about activities that interfere with the device,[14] and feel unsafe when performing routine tasks.[9]

Although families overprotect patients with PPM, patients with PPMs desire to learn more activities, driving restrictions, sexual relationships, and sociability.[15] Moreover, the strict regulation of coronavirus disease (COVID-19) prevention has decreased their PA since 2020.[16] This restriction prevents patients with PPM from participating in any activities.

This limitation causes the deterioration of the physical performance of patients with PPMs. The condition of the heart and blood vessels worsens, and the death rate increases.[17, 18] Patients with PPMs feel depressed,[12] and caregivers feel burdened.[19, 20] Conversely, patients with sufficient PAs would have a healthy cardiovascular system, greater mobility, and reduced frailty.[21] Moreover, engaging in sufficient PAs could prevent further the incidence of chronic noncommunicable diseases, lower depression, and improve the quality of life.[22, 23]

Previous Thai studies have reported on the living experiences, quality of life, self-care habits, and health behaviors of patients with PPMs. To the best of our knowledge, no study has evaluated the PA levels of patients with PPMs. However, some studies on PA in patients with heart diseases who underwent surgery have included data on the implantation of an automated implantable cardioverter-defibrillator (AICD),[24] coronary artery catheterization (percutaneous coronary intervention [PCI]),[25, 26] and coronary artery bypass surgery (CABG).[27]

Thus, factors identified in the literature review and Pender's conceptual framework associated with PA, exercise habits, and health behaviors must be examined. Age, perceived self-efficacy, perceived benefits, perceived barriers, social support, and health literacy presented basic knowledge regarding PA in patients with PPMs. This study adds a nursing plan to encourage patients to engage in PAs within the appropriate level that patients with PPMs should perform.

This study aimed to investigate the PA of patients with PPMs and identify PA-related factors in patients with PPMs based on age, perceived self-efficacy, perceived benefits, perceived barriers, social support, and health literacy.

Materials and methods

Study subjects

This descriptive and correlational study enrolled male and female patients with PPMs aged > 18 years who visited the pacemaker clinic of three tertiary care hospitals in Bangkok, Thailand.

Patients with PPMs aged > 60 years with no dementia or other serious neurological diseases, ability to understand and communicate in Thai, and willingness to participate in the study were recruited. However, patients with PPMs having significant arrhythmia or heart failure, those with AICD or cardiac resynchronization therapy defibrillator, and those who experienced chest pain, palpitations, dizziness, and difficulty breathing while providing information were excluded from the study.

The sample size and test power were determined based on the G*Power program. The effect size of 0.3 was calculated by averaging the total Pearson correlation coefficients of the variables reported by Tongtiam W, Wannapo P, *et al.*, Won MH, Son YJ, and Crawford RS, *et al.*[24 - 27] The power of the test was 0.8, the significance level was 0.05, and a two-tailed test was used. Initially, the calculated sample size was 84. However, to account for potential sample loss and missing data, the sample size was increased by 20.0%, resulting in a total of 110 samples for inclusion.

Measurements

Seven instruments were employed for data collection: 1) The demographic questionnaire was developed by the researchers and composed of 17 items of patient data and 6 items on health status; 2) The PA questionnaire was adapted from the Duke activity status index[28] with permission and minor wording modifications to fit for patients with PPMs. The translated version was used with permission.[29] The questionnaire was composed of 12 statements with responses of "could do," "could not do," and "did not

do," as well as the frequency and duration of each activity. The content validity index (CVI) and Cronbach's alpha coefficient of this questionnaire were 1.0 and 0.76, respectively. The score ranges from 0 to 12, with a high score indicating that patients with PPMs are more physically active; 3) The self-efficacy of the PA questionnaire and self-efficacy questionnaire in re-hospitalized patients with acute myocardial infarction (AMI) undergoing PCI were also employed.[29] It consists of 10 positive questions with a 10-point rating scale ranging from 0 (not confident) to 10 (very confident). The CVI and Cronbach's alpha coefficient of this questionnaire were 1.0 and 0.88, respectively. The score was between 0 and 100, and a high score indicated that the patient with PPM had a high perceived self-efficacy in PA; 4) The perceived benefit of the PA questionnaire was developed with permission from the developers of the perceived benefit of the PA questionnaire in re-hospitalized patients with AMI undergoing PCI[29] based on Pender's health-promotion concept. It includes 30 positive items regarding the advantages of PA. The 4-point rating scale was "strongly agree," "agree," "disagree," and "strongly disagree." The CVI and Cronbach's alpha coefficient of this questionnaire were 1.0 and 0.95, respectively. The score was between 0 and 90, with a high score indicating that patients with PPMs have a high perceived benefit of PA; 5) The perceived barrier of the PA questionnaire was developed with permission from the makers of the perceived barrier of the PA questionnaire.[29] All 14 negative items were evaluated using a 4-point rating scale of "strongly agree," "agree," "disagree," and "strongly disagree." The CVI and Cronbach's alpha coefficient of this questionnaire were 1.0 and 0.8, respectively. The scores ranged from 0 to 42. Patients with PPMs with high scores had more significant perceived PA limitations; 6) The social support for PA scale was developed social support scale for PA in patients with new coronary artery disease (CAD) undergoing PCI with permission from Raungratanaamporn S, *et al*.[30] The 5-point Likert scale was "never," "rarely," "2 - 3 times," "often," and "always." The questionnaire was composed of 11 positive items and 1 negative item. The CVI and Cronbach's alpha coefficient of this questionnaire were 1.0 and 0.9, respectively. The scores ranged from 0 to 48 points; a high score indicated that patients with PPMs received high social support from their families or friends; and 7) The PA-health literacy questionnaire was adapted with permission from the health literacy tool in patients with AMI undergoing CAG by Wanpho P, *et al*.[25] It has a total of 14 positive items and a 4-point rating scale of "never," "for a long time," "sometimes," and "always." The CVI and Cronbach's alpha coefficient of this questionnaire were 1.0 and 0.87, respectively. The scores ranged from 0 to 56 points. A high score indicated that patients with PPMs have high PA-health literacy.

We were permitted by the proprietors of all questionnaires to adapt and modify the items to suit to patients with PPMs. Content validity was checked by five specialists (a cardiologist, a nurse professor, and three cardiology-APNs). Subsequently, the reliability was evaluated in a study involving 30 patients with PPMs, such as the pacemaker clinic samples of Pramongkutklao Hospital.

Data collection

Overall, 110 participants were recruited using the multistage sampling technique from pacemaker clinics at Ramathibodi Hospital, Phramongkutklao Hospital, and Police Hospital between June 13 and September 30, 2022.

Ethical considerations

Institutional review board (IRB) approval was obtained from the Human Research Ethics Committee of the Faculty of Medicine of the Ramathibodi Hospital (COA. MURA no. 2022/382), IRB of the Royal Thai Army Medical Department (IRBRTA no. 0740/2565), and ethics committee of Police Hospital (Oq53/65), Bangkok, Thailand. The researcher provided an overview of the study. The participants were voluntarily invited to take part in the study, and they provided written informed consent. All participant information was kept confidential and anonymous.

Statistical analysis

IBM SPSS Statistics for Windows version 28.0 (IBM Corp., Armonk, NY, USA) was used in the data analysis. The statistical significance level was set at $P < 0.05$, and data were evaluated in the following order. Descriptive statistics were used to examine the demographic data and studied variables, such as frequency, percentage, mean, median, mode, minimum, maximum, and standard deviation. The normality of the data distribution of the variables was evaluated using the permissible skewness and kurtosis index between + 1.96 and - 1.96, according to the

preliminary agreement in calculating Pearson's correlation. However, age, perceived benefit, social support, and health literacy with skewness and kurtosis scores out of the range of - 1.96 and + 1.96 had non-normal data distribution.[31] As a result, Pearson's correlation coefficient was not used to calculate these variables. Pearson's product–moment correlation was used to explore the association between perceived self-efficacy and perceived barriers to PA in patients with PPMs. Spearman rank-order correlation was used to examine the age, perceived benefits, social support, and health literacy of individuals with PPM.

Results

Participant characteristics

Of the 110 participants, most were female (51.8%) and between 71 and 80 years old (31.8%). The mean participant age was 67.4 (SD = 15.0) years. On average, the waist circumference measured 85.9 cm, and 37.3% of the participants had a normal body mass index, 62.7% were married, 30% graduated with a bachelor's degree, 35.5% were unemployed, 74.5% did not commute to work, 68.1% earned enough to pay off their costs, 90.9% lived with family or relatives, 90.0% had a caregiver, and 47.0% had offspring as carvers. Moreover, 33.7% of the participants had sick sinus syndrome, 98.2% had comorbidities with hypertension (24.5%), 75.5% had been inserted a dual-chamber PPM, 69.1% were first-time PPM users, 19.1% had implantation for 4–11 months, 96.4% had no complications after implantation, 96.3% were engaged in PA before the procedure, and 100.0% had PA after PPM (**Tables 1 - 3)**.

Before the procedure, 23.2% of the participants walked > 1 km, indicating the highest PA level, 13.2% engaged in moderate exercise, and 9.3% engaged in cooking. After PPM implantation, 23.1% of the participants had the highest PA of walking for > 1 km, 12.9% did moderate housework, and 11.5% performed moderate exercise. In contrast, the lowest PA after PPM was observed for heavy exercise (0.0%), lifting (2.1%), and gardening/farming (2.5%) (**Figure 1)**.

Characteristics of the variables

Patients with PPM had an average PA score of 6.8 (56.8%, SD = 2.3), the total energy used for PA was 26.3 MET (SD = 11.4), the frequency of PA was 114.5 time/week (median = 100, mode = 70, SD = 53.9), and the duration of PA was 114.1 min/time (median = 95.5, mode = 50.0, SD = 78.8).

In addition, the participants had an average perceived PA self-efficacy score of 63.9 (SD = 17.3), perceived PA benefits of 95.9 (SD = 9.7), perceived PA barriers of 25.9 (SD = 5.5), social support for PA of 32.7 (SD = 8.9), and PA-health literacy of 38.0 (SD = 9.3).

The PA level of patients with PPMs was 56.8%. The highest to lowest percentages of variables' mean scores were perceived PA benefit (79.9%), PA-health literacy (67.8%), perceived self-efficacy (63.9%), social support (54.5%), and perceived PA barriers (46.2%) (**Figure 2).**

Correlation between age, perceived self-efficacy, perceived benefits, perceived barriers, social support, health literacy, and PA of patients with PPMs

The data analysis demonstrated the relationship between age, perceived self-efficacy, perceived benefits, perceived barriers, social support, and health literacy with PA in patients with PPMs. The perceived PA self-efficacy, perceived PA benefits, social support, and PA-health literacy demonstrated statistically significant positive correlations with PA in patients with PPM at 0.05 (r = 0.448, *Spearman's rho* = 0.339, 0.217, and 0.459, respectively). Age and perceived PA barriers were significantly negatively correlated with PA in patients with PPMs at 0.05 (*Spearman's rho* = - 0.467 and r = - 0.312, respectively), as shown in **Table 4.**

Table 1. Demographic data of participants (n = 110).

Data	Min	Max	Mean	SD
Age (year)	19	95	67.4	14.9
Weight (kg)	43	110	65.0	13.4
Waist (cm)	63	114	85.9	10.6
Height (cm)	144	184	161.0	8.4

Table 2. Demographic data of participants (n = 110).

Data	N	Percentage
Age (year)		
≤ 30	3	2.7
31 - 40	4	3.6
41 - 50	8	7.3
51 - 60	10	9.1
61 - 70	32	29.1
71 - 80	35	31.8
≥81	18	16.4
Gender		
Male	53	48.2
Female	57	51.8
BMI (kg/m^2)		
Underweight	4	3.6
Normal range	41	37.3
Overweight	15	13.7
Obese 1	34	30.9
Obese 2	16	14.5
Occupation		
None	39	35.5
Government	38	34.5
Own business	7	6.4
Merchant	7	6.4
Company employee	6	5.5
General employee	5	4.5
State enterprise	4	3.6
Agriculturist	3	2.7
Student	1	0.9
Characteristic of work/ daily life		
Sitting	56	50.9
Standing/ Walking	50	45.5
Heavy working	4	3.6
Caregiver		
None	11	10.0
Have caregiver	99	90.0
(Can answer > 1) (n = 115)		
Children	54	47.0
Husband/ wife	46	40.0
Grandchild	7	6.1
Parents	4	3.5
Sibling	2	1.7
Friend	2	1.7

Table 3. Characteristics of PPM insertion (n = 110).

Data	N	Percentage
Diagnosis		
Sick sinus syndrome	37	33.7
Third AV block	23	20.9
Battery replacement	23	20.9
Atrial fibrillation	13	11.8
Second AV Block	6	5.5
Sinus bradycardia/ sinus pause	4	3.6
First AV block	2	1.8
Revise lead	2	1.8
Type		
Single chamber	27	24.5
Dual chamber	83	75.5
Time		
First	27	24.5
Second	19	17.3
Third	12	10.9
Fourth	3	2.7
Duration		
7 days	2	1.8
1 - 3 months	10	9.1
4 - 11 months	21	19.1
1 year	11	10.0
2 years	15	13.6
3 years	15	13.6
4 years	10	9.1
5 years	8	7.3
> 5 years	18	16.4
Complication		
None	106	96.4
Have complication	4	3.6

Table 4. Correlation between the variables and PA (n = 110).

	Pearson's correlation			Spearman's rho		
	Perceived self-efficacy	Perceived barriers	Age	Perceived benefits	Social support	Health literacy
Physical activity	0.448**	- 0.312**	- 0.467**	0.339**	0.217*	0.459**

* Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.01 level (2-tailed).

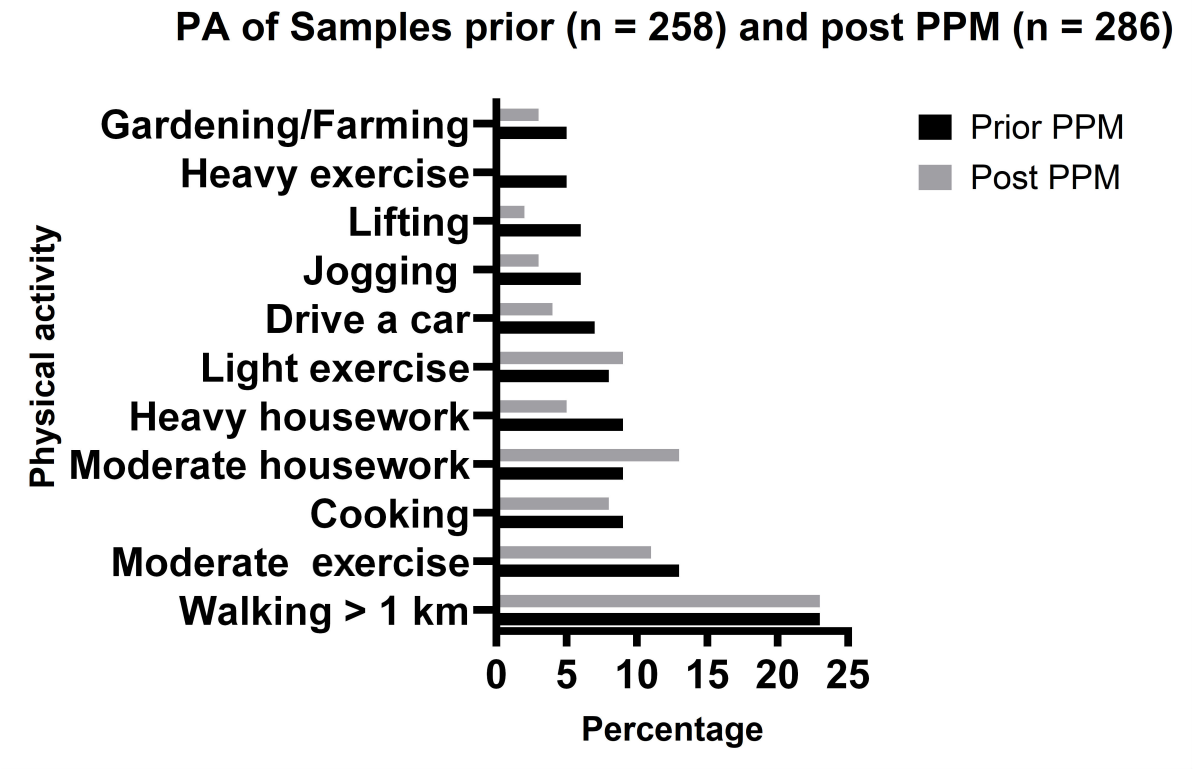

Figure 1. PA of samples prior (n = 258) and post PPM (n = 286).

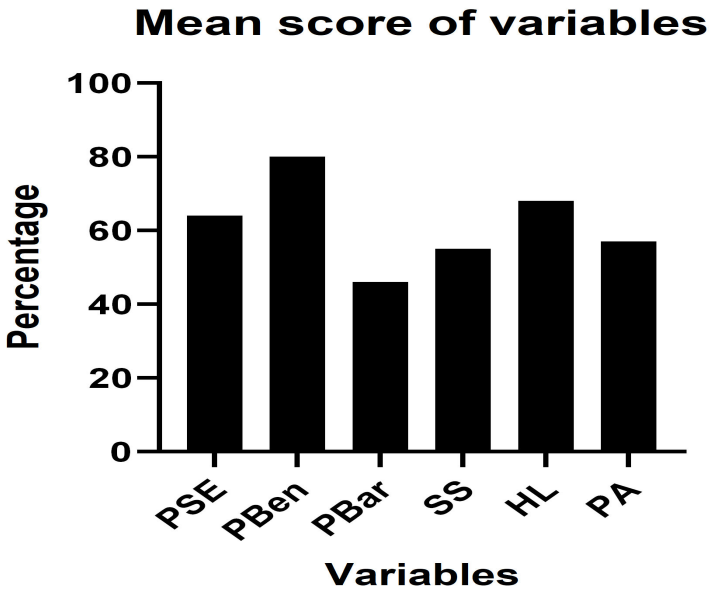

Figure 2. Mean score of variables (n = 110)
PSE, Perceived self-efficacy; PBen, Perceived benefits; Pbar, perceived barriers; SS, Social support; HL, Health literacy; PA, Physical activity.

Discussion

According to the wear and tear theory, aging is a natural process caused by the use of organs over a long period or being too heavily used as someone ages, leading to the loss of cells, tissues, and organs and worsening the condition of several systems in the body. As age increases, several progressive illnesses emerge.[32] Thus, most older people have underlying diseases, such as hypertension, heart disease, and brain disease, which limits PA. In this study, a significant number of participants were older, retired, had comorbidities, and had no job, resulting in a reduced capacity to perform different PAs, which led to performing PAs in the form of daily activities, housework, and gardening. Consequently, their PA levels were moderate. Therefore, age is significantly negatively correlated with PA in patients with PPMs. This outcome is consistent with that of Chala-em T, *et al*. who reported that age was related to geriatric PA and that PA decreased as people grew older.[33] This is also consistent with the findings of Crawford RS who discovered that age was negatively correlated with PA in patients with AICD,[24] and Raungrattanaamporn S, *et al*. discovered that age was negatively associated with PA in patients with new CAD who were diagnosed using coronary angiography.[30]

Self-efficacy is an essential motivation for a person to demonstrate good and proper behavior. It is more likely to inspire people to achieve their goal behaviors than persons who feel and incompetent.[5] This study revealed that the perceived self-efficacy of patients with PPM showed a significantly moderate positive correlation with their PA. Furthermore, most participants were confident in doing PA despite having to do it mostly alone, in an unpleasant weather, and feeling slight muscle pain. However, participants were less satisfied with having sex. Thus, when the participants have a high perceived self-efficacy, they will have confidence in their ability to perform various activities to achieve their goals and perform physical activities better. This is consistent with the findings of Crawford RS who discovered that self-efficacy was associated with PAs in patients with AICD,[24] Tongtiam W. who found that self-efficacy was positively correlated with PA in patients with CAD after CABG,[27] Won MH and Son YJ. who documented that self-efficacy was associated with PA in patients with CAD undergoing PCI,[26] and Wannapo P, *et al*. who discovered that self-efficacy was positively correlated with PA in patients with AMI undergoing CAG.[25]

Perceived benefit refers to the feeling, understanding, or perception of various aspects of people that can potentially prevent harm or complications. If a person believes that acting will prevent the disease or illness from occurring, perceived benefit guides the individual's activity choices, and the person strictly follows the instructions.[5] This study reported a statistically significant positive correlation between perceived benefits and PA in patients with PPMs. Furthermore, the participants had the best attitude toward PA, which encouraged PA in patients who underwent cardiac surgery. Likewise, they were aware that PA improved their mental health, muscle strength, physical strength, and physical performance. Consequently, individuals who perceived PA as beneficial were more inclined to engage in higher PA levels. This finding is consistent with the results of Chaiyawut P, who reported a positive correlation between perceived benefits and exercise behavior in patients with AMI after PCI or CABG.[34] Moreover, Tongtiam W. found that the perceived benefit was positively correlated with PA in patients with CAD after CABG, which could significantly predict the PA levels of patients.[27]

Perceived barriers are believed to impede engagement in health-promoting behaviors. When individuals perceive multiple obstacles to taking action, they are more likely to disengage in the activity.[5] This study conveyed that perceived barriers had a moderate negative correlation with the PA of patients with PPMs, showing statistical significance. The participants reported experiencing high levels of fatigue, tiredness, limited PA, and a lack of access to PA facilities. Thus, when the participants perceived greater difficulty in performing PAs, their level of engagement decreased accordingly. This finding is consistent with the results of Chaiyawut P, who found that perceived barriers were negatively correlated with exercise behaviors in patients with AMI undergoing PCI or CABG.[34] Similarly, Tongtiam W. found that perceived barriers were negatively correlated with PA in patients with CAD after undergoing CABG.[27] Furthermore, the data were collected during the COVID-19 epidemic, which imposed strict restrictions beginning in 2020. This barrier leads to reduced PA.

Social support encompasses acceptance, love, value, and a sense of self-worth from others and provision of emotional support, material resources,

information, and advice, enabling individuals to effectively integrate into society.[5] This study revealed that social support had a statistically significant low positive correlation with the PA of patients with PPMs. Furthermore, the families of the participants encouraged or supported them to engage in PA. As a result, they were rewarded for PA, which increased their motivation to engage in PA. Participants who were married, lived with a family, and had a caregiver who was either their children or spouse received family support for self-care and activities after PPM implantation. Consequently, participants who received sufficient social support for PA were more likely to adhere to the treatment plan and increase their PA levels. This finding was consistent with that of Chaiyawut P, who discovered a positive relationship between social support and exercise behavior in patients with AMI undergoing PCI or CABG.[34] Thitikul M, *et al.* discovered that social support was related to exercise behavior in patients with AMI undergoing PCI.[35] Won MH and Son YJ. revealed that social support was related to PA in patients with CAD undergoing CAG.[26] Moreover, Pankam T, *et al.* discovered a positive correlation between social support and health behaviors in patients with PPM.[36] Wannapo P, *et al.* found a positive correlation between social support and PA in patients with AMI undergoing PCI.[25]

Health literacy involves accessing, understanding, applying, and effectively communicating accurate health information to promote and maintain good health.[37] A person with sufficient health literacy can understand, access, evaluate, use, and communicate health information accurately. Consequently, PA has been increased to promote and maintain good health. In this study, health literacy demonstrated a significant positive relationship with PA in patients with PPMs. In addition, participants adhered to PA recommendations provided by healthcare professionals, demonstrated an understanding of pertinent PA information, and exercised caution before engaging in PA. However, they exhibited reduced documentation of PA and abnormal symptoms, shared limited PA information with others, and less utilized PA manuals. Consequently, older adults, who typically have lower health literacy, may face challenges in understanding, analyzing, accessing PA-related information, interacting with others, and making informed decisions regarding PA compared with younger individuals.[38] Most participants were older, with an average age of 67.4 years, so they may have had slower learning abilities. In addition, as participants received their first PPM within 4 - 11 months, lacking previous experience with pacemaker insertion, they may have required greater knowledge regarding appropriate PA. Thus, the participants with higher health literacy levels had increased engagement in PA. This finding is supported by data reported by Wannapo P, *et al*, who found that health literacy was positively correlated with PA in patients with AMI undergoing PCI.[25]

This study is limited by the wide age range of the participants (19 - 97 years) and the predominantly older participant population, who may have imitated PA behaviors. This aspect could potentially introduce selective factors that influence specific data distribution, leading to non-normal distributions.

The findings of this study were similar to those of previous research following the discussion because the factors were selected from the Pender health-promoting model and a literature review of patients with heart disease who underwent heart procedures. This finding was similar to that observed in patients who underwent PPMs under underlying conditions. Furthermore, most participants were older and had comparable comorbidities. Thus, it is close to the sample group examined in the present study, resulting in consistent research results for all variables in the same direction.

Conclusion

Perceived self-efficacy, perceived benefits, perceived barriers, social support, health literacy, and age are significant factors related to the PA of patients with PPMs. As implications for nursing practice, nurses should encourage patients with PPMs to improve their PA to achieve better-perceived self-efficacy, perceived benefits, social support, and health literacy. In addition, older patients with PPMs and those who have negatively perceived barriers should be motivated to increase their PA. Further study is needed to focus on the factors that predict PA in patients with PPMs and test the effectiveness of an intervention program for increasing and personalizing PA in patients with PPMs.

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Conflicts of interest statement

The author had completed an ICMJE disclosure form. No any potential or actual relationship, activity or interest related to the content of this article.

Data sharing statement

All data generated or analyzed during the present study are included in this published article. Further details, opinions, and interpretations are available from the corresponding author on reasonable request.

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