ปัจจัยเสี่ยงของภาวะหัวใจห้องบนเต้นเร็วผิดปกติในผู้ป่วยที่ได้รับการรักษาด้วยเครื่องกระตุ้นหัวใจแบบถาวรในสถาบันโรคทรวงอก

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หน่วยสรีระไฟฟ้าหัวใจ กลุ่มงานอายุรศาสตร์หัวใจ สถาบันโรคทรวงอก
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Predisposing Factors of Atrial High-rate Episodes in Patients with Permanent Pacemaker Implantation in Central Chest Institute of Thailand

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Abstract

Background: The atrial high-rate episodes (AHREs) are considered clinically correlated with atrial fibrillation (AF). Moreover, the stroke risk is increasing following the AHREs burden and/or CHA_2DS_2-VASc score. However, the predisposing factors of the AHREs were not clearly known. **Objective:** To investigate the predisposing factors of AHREs in patients with dual-chamber pacemakers. **Method:** This study was a retrospective observational study recruiting patients without history of AF prior to the dual-chamber pacemaker implantation. Patients with evidences of other atrial tachyarrhythmias prior to the dual-chamber pacemaker implantation were excluded. The baseline demographic data, past medical history, medications, echocardiographic parameters, electrocardiographic findings and pacemaker interrogation data were analyzed and compared between patients with and without AHREs. Predisposing factors predicting AHREs was analyzed by using univariate and multivariate logistic regression analysis. **Result:** A total of 239 patients undergoing dual-chamber pacemaker implantation in Central Chest Institute of Thailand among January 2017 to December 2021 were recruited. The data of 117 patients from 239 patients were analyzed. There were 89 patients had no AHREs and 28 patients had AHREs. Multivariate logistic regression analysis showed that the percentage of atrial pacing was significantly greater in patients with AHREs (odds ratio 1.02; 95% CI 1.003 to 1.041; p-value = .021). **Conclusion:** Increased atrial pacing was the only predisposing factor of AHREs in Thai patients with permanent pacemaker. However, larger prospective study should be studied in the future.

Keywords: AHREs, Atrial fibrillation, Pacemaker, Stroke, Predisposing factors

บทคัดย่อ

ภูมิหลัง: ภาวะหัวใจห้องบนเต้นเร็วผิดปกติได้รับการพิจารณาว่ามีความสัมพันธ์ทางคลินิกต่อการเกิดหัวใจห้องบนสั่นพลิ้ว นอกจากนี้ ความเสี่ยงต่อการเกิดสมองขาดเลือดยังเพิ่มขึ้นตามภาวะหัวใจห้องบนเต้นเร็วผิดปกติและ/หรือระดับคะแนนของ CHA_2DS_2-VASc ที่เพิ่มขึ้น อย่างไรก็ตาม ปัจจัยที่ส่งเสริมให้เกิดภาวะหัวใจห้องบนเต้นเร็วผิดปกติยังไม่เป็นที่ทราบแน่ชัด **วัตถุประสงค์:**

เพื่อศึกษาปัจจัยที่ส่งเสริมการเกิดภาวะหัวใจห้องบนเต้นเร็วผิดปกติในผู้ป่วยที่ใส่เครื่องกระตุ้นหัวใจแบบสองห้อง **วิธีการ:** การศึกษานี้เป็นการศึกษาแบบสังเกตการณ์ย้อนหลังในผู้ป่วยที่ไม่ได้มีประวัติเป็นหัวใจห้องบนสั่นพลิ้วมาก่อนใส่เครื่องกระตุ้นหัวใจแบบสองห้อง ผู้ป่วยที่ตรวจพบหัวใจห้องบนผิดจังหวะชนิดอื่น ๆ จะได้รับการตัดออกจากการศึกษา ข้อมูลผู้ป่วยพื้นฐาน, ประวัติโรคประจำตัว, ยาที่ได้รับ, ผลการตรวจคลื่นเสียงสะท้อนหัวใจ, ผลการตรวจคลื่นไฟฟ้าหัวใจ และข้อมูลการตรวจเครื่องกระตุ้นหัวใจได้รับการวิเคราะห์และเปรียบเทียบระหว่างผู้ป่วยที่มีและไม่มีภาวะหัวใจห้องบนเต้นเร็วผิดปกติ ปัจจัยส่งเสริมที่ทำนายการเกิดภาวะหัวใจห้องบนเต้นเร็วผิดปกติได้รับการวิเคราะห์โดยใช้การวิเคราะห์ถดถอยเอกนามและพหุนาม **ผล:** ผู้ป่วยจำนวน 239 คนที่ได้รับการใส่เครื่องกระตุ้นหัวใจแบบสองห้องในสถาบันโรคทรวงอกระหว่างมกราคม พ.ศ. 2560 ถึงธันวาคม พ.ศ. 2564 ได้รับการคัดเลือกเข้าสู่การศึกษา ข้อมูลของผู้ป่วยจำนวน 117 คน จากผู้ป่วยทั้งหมด 239 คน ได้รับการวิเคราะห์ โดยมีผู้ป่วยจำนวน 89 คนที่ไม่มีภาวะหัวใจห้องบนเต้นเร็วผิดปกติและ 28 คนที่มีภาวะหัวใจห้องบนเต้นเร็วผิดปกติ การวิเคราะห์ถดถอยพหุนามแสดงให้เห็นว่าเปอร์เซ็นต์ของการกระตุ้นหัวใจห้องบนมากกว่าในกลุ่มผู้ป่วยที่มีภาวะหัวใจห้องบนเต้นเร็วผิดปกติอย่างมีนัยสำคัญทางสถิติ (odds ratio 1.02; 95% CI 1.003 to 1.041; p-value = .021) **สรุป:** การกระตุ้นหัวใจห้องบนที่เพิ่มขึ้นเป็นปัจจัยส่งเสริมเดียวต่อการเกิดภาวะหัวใจห้องบนเต้นเร็วผิดปกติในผู้ป่วยไทยที่ใส่เครื่องกระตุ้นหัวใจแบบถาวร อย่างไรก็ตาม การศึกษาแบบไปข้างหน้าขนาดใหญ่ควรมีการศึกษาต่อไปในอนาคต

คำสำคัญ: ภาวะหัวใจห้องบนเต้นเร็วผิดปกติ, หัวใจห้องบนสั่นพลิ้ว, เครื่องกระตุ้นหัวใจ, สมองขาดเลือด, ปัจจัยส่งเสริม

Introduction

The cardiac implantable electronic devices (CIEDs) have been introduced in 1958 by C.W. Lillehei and Earl Bakken for bradycardia treatment and developed for anti-tachycardia therapy in 1980 by Michael Morchower.[1, 2] The permanent pacemakers is CIEDs designed for bradyarrhythmia treatment.[3, 4] Moreover, the permanent pacemaker also has the sensing function for detection of all of the cardiac intrinsic activities and stored in number of arrhythmic events, time, duration, intracardiac electrogram.[5]

The atrial high-rate episodes (AHREs) are considered clinically correlated with atrial fibrillation (AF)[6-8, 10] About 10-30% of patients without AF have AHREs increasing risk of stroke for 0.8-1% per year.[9, 11-12]

To date, the definition of AHREs is not well-defined. According to the European Society of Cardiology (ESC) guidelines, AHREs are defined as the atrial rate ≥ 175 beat per minute for at least 5 minutes.[7] Moreover, the stroke risk is increasing following the AHREs burden and/or CHA_2DS_2-VASc score.[7]

Previous study has shown that age, sick sinus syndrome, and the percentage of atrial pacing in patients with dual-chamber pacemaker could predict risk of AHREs.[13] However, there has been scarce data of factors predicting AHREs in Thailand. This study was conducted to investigate the predisposing factors of AHREs in patients with dual-chamber pacemakers.

Materials and Methods

This study was a retrospective observational study recruiting patients aged ≥ 18 years old without history of atrial fibrillation (AF) prior to the dual-chamber pacemaker implantation. Patients with evidences of other atrial tachyarrhythmias prior to the dual-chamber pacemaker implantation were excluded. The study protocol was approved by Human Research Ethics Committee of Central Chest Institute of Thailand. This study was conducted in accordance with the Declaration of Helsinki and the International Conference on Harmonization for Good Clinical Practice Guidelines.

The baseline demographic data, past medical history, medications, echocardiographic parameters, electrocardiographic findings and pacemaker interrogation data were collected from medical records and analyzed between patients with and without AHREs. The AHREs

were defined as the atrial rate ≥ 175 beat per minute for at least 5 minutes according to the 2020 ESC guidelines.[7]

The categorical data are presented as frequency and percentage. The continuous data are presented as mean and standard deviation (SD). The comparison of categorical data between patients with and without AHREs was analyzed by using chi-square test or Fisher's exact test. The comparison of continuous data between 2 groups was performed by using student t-test. Predisposing factors predicting AHREs was analyzed by using univariate and multivariate logistic regression analysis. The p-value < .05 was considered the statistical significance.

Results

A total of 239 patients undergoing dual-chamber pacemaker implantation in Central Chest Institute of Thailand among January 2017 to December 2021 were recruited. Of note, 75 patients were not meet the inclusion criteria because of history of AF, atrial flutter, other atrial tachyarrhythmias before dual-chamber pacemaker implantation or pacemaker implantation from other hospitals and 47 patients had insufficient record because patients were lost to follow up or death, loss of medical records or electrogram. The data of 117 patients from 239 patients were analyzed. There were 89 patients had no AHREs and 28 patients had AHREs (Figure 1). About 60% of patients was females and the average age was 63.75 years. The average body mass index (BMI) was 24.42 kg/m^2. About 80% of patients had hypertension and dyslipidemia. The indication for pacemaker implantation was complete atrioventricular (AV) block (60.68%), sinus node dysfunction (26.50%), and second-degree AV block (12.82%). An average left ventricular ejection fraction (LVEF) was 66.73%. An average percentage of atrial and ventricular pacing were 29.92 % and 72.73%, respectively (Table 1). The baseline demographic data were comparable between patients with and without AHREs.

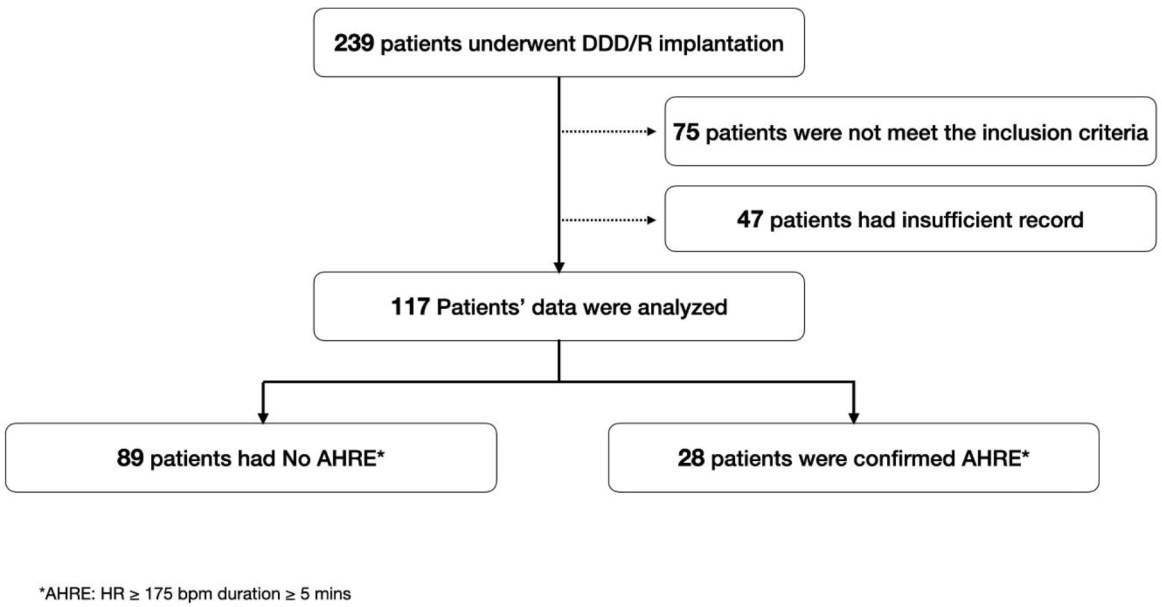

Figure 1. Flow diagram illustrating patient selection and recruitment

Table 1 Baseline characteristics of the patients.

Demographic data	All patients (n = 117)	No AHREs (n = 89)	AHREs (n = 28)	p-value
Age (years)	63.75±12.93	64.48±12.88	61.42±13.03	.277
Male sex, n (%)	49 (41.88)	37 (41.57)	12 (42.86)	.904
Body mass index	24.42±4.25	24.69±4.40	23.53±3.66	.207
Medical history, n (%)				
- Diabetes mellitus	41 (35.04)	33 (37.08)	8 (28.57)	.411
- Hypertension	84 (71.79)	66 (74.16)	18 (64.29)	.311
- Dyslipidemia	78 (66.67)	59 (66.29)	19 (67.86)	.878
- Heart failure	7 (5.98)	5 (5.62)	2 (7.14)	.672
- Stroke/TIA	7 (5.98)	5 (5.62)	2 (7.14)	.672
- Vascular disease	24 (20.51)	21 (23.60)	3 (10.71)	.141
- Chronic kidney disease	13 (11.11)	11 (12.36)	2 (7.14)	.731
CHA_2DS_2-VASc score, n (%)				
- 0	14 (11.97)	9 (10.11)	5 (17.86)	.559
- 1	17 (14.53)	13 (14.61)	4 (14.29)	
- ≥2	86 (73.50)	67 (75.28)	19 (67.86)	
Medication, n (%)				
- Aspirin	41 (35.04)	34 (38.20)	7 (25.00)	.202
- $P2Y_{12}$ inhibitors	16 (13.68)	13 (14.61)	3 (10.71)	.759
- Beta-blockers	14 (11.97)	11 (12.36)	3 (10.71)	>.99
- NDCCB	1 (0.85)	1 (1.12)	0 (0)	>.99
ECG findings				
- Intrinsic QRS duration (msec)	113.12±31.47	112.30±32.95	115.75±26.60	.615
- Paced QRS duration (msec)	140.52±33.79	139.01±31.79	145.35±39.74	.388
Echocardiographic parameters				
- LVEF (%)	66.73±10.19	66.88±10.45	66.26±9.47	.778
- LA dimension (mm)	37.99±7.73	37.64±7.63	39.10±8.08	.385
Indication of pacemaker, n (%)				
- Sinus node dysfunction	31 (26.50)	22 (24.72)	9 (32.14)	.394
- Second-degree AV block	15 (12.82)	10 (11.24)	5 (17.86)	
- Complete AV block	71 (60.68)	57 (64.04)	14 (50.00)	
Percentage of pacing (%)				
- Atrial pacing, mean±SD	29.92±32.96	26.71±30.95	40.14±37.45	.059
- Ventricular pacing, mean±SD	72.73±40.44	71.75±40.83	75.86±39.74	.640

AHREs = atrial high-rate episodes, TIA = transient ischemic attack, NDCCB = non-dihydropyridine calcium channel blocker, ECG = electrocardiography, LVEF = left ventricular ejection fraction, LA = left atrium, AV block = atrioventricular block.

Multivariate logistic regression analysis showed that the percentage of atrial pacing was significantly greater in patients with AHREs (odds ratio [OR] 1.02; 95% confidence interval 1.00 to 1.04; p-value = .021) (Table 2).

Table 2 Predictors of AHREs in patients with permanent pacemaker.

Predictors	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p-value	OR (95%CI)	p-value
Age	0.98 (0.95, 1.01)	.278	0.99 (0.95, 1.04)	.748
Male sex	0.95 (0.40, 2.24)	.904		
BMI	0.93 (0.83, 1.03)	.207	0.92 (0.81, 1.03)	.143
Diabetes mellitus	0.68 (0.27, 1.71)	.412	2.45 (0.59, 10.20)	.217
Hypertension	0.63 (0.25, 1.55)	.314	0.91 (0.23, 3.55)	.887
Dyslipidemia	1.07 (0.43, 2.66)	.878		
Heart failure	1.29 (0.24, 7.06)	.767	0.82 (0.07, 9.64)	.877
Stroke/TIA	1.29 (0.24, 7.06)	.767		
Vascular disease	0.39 (0.11, 1.42)	.152	0.39 (0.11, 1.42)	.228
CKD	0.55 (0.11, 2.62)	.449		
CHA_2DS_2-VASc ≥ 2	0.51 (0.15, 1.70)	.274	1.13 (0.22, 5.75)	.879
Intrinsic QRS duration	1.00 (0.99, 1.02)	.612	1.00 (0.98, 1.02)	.992
Paced QRS duration	1.01 (0.99, 1.02)	0.386	1.01 (0.99, 1.03)	.332
LVEF (%)	0.99 (0.95, 1.04)	.776	1.00 (0.95-1.05)	.937
LA dimension	1.03 (0.97, 1.09)	.383	1.05 (0.98-1.13)	.184
Second-degree AVB	1.22 (0.33, 4.60)	.766		
Complete AVB	0.60 (0.23, 1.59)	.303		
Atrial pacing	1.01 (1.00, 1.02)	.063	1.02 (1.003-1.041)	.021*
Ventricular pacing	1.00 (0.99, 1.01)	.638	1.01 (0.99-1.03)	.305

AHREs = atrial high-rate episodes, OR = odds ratio, 95% CI = 95% confidence interval, BMI = body mass index, TIA = transient ischemic attack, CKD = chronic kidney disease, LVEF = left ventricular ejection fraction, LA = left atrium, AVB = atrioventricular block. * $P < .05$ was considered as statistical significance.

Discussion

This study illustrated the percentage of atrial pacing was associated with increasing rate of AHREs in patients with dual-chamber pacemaker with statistical significance. The average percentage of atrial pacing in patients with and/or without AHREs in this trial were 40% and 26%, respectively. Further study for investigating how much percentages of atrial pacing will increase the risk of AHREs in those patients.

Previous study showed the increased rates of AHREs > 6 hours were associated with the higher risk of thromboembolism based on CHA_2DS_2-VASc score.[14] Furthermore, there was previous trial demonstrating increased age, left atrial (LA) dimension and blood pressure have been the predictors of subclinical atrial fibrillation in patients ≥ 65 years of age.[15] However, no study was investigated in terms of the percentage of atrial and/or ventricular pacing.

The baseline demographic data including age, sex, BMI, medical history, CHA_2DS_2-VASc score and LA dimension in this trial were comparable between patients with and without AHREs. Although previous study has shown that age, and the percentage of atrial pacing in patients with dual-chamber pacemaker could predict risk of AHREs,[13] multivariate logistic regression analysis in this study has shown that only the percentage of atrial pacing could predict AHREs in those patients.

However, this study had some limitations. First, this study was a retrospective observational study conducting in a single center. There may

be a missing data in medical records. Second, this study had small sample size and short observation time leading to the low event rate. Nevertheless, this was the first trial showing the percentage of atrial pacing could predict AHREs. Finally, this study was conducted in only Thai patients leading to limit generalizable to other racial patients. However, larger study should be conducted in other racial patients in the future.

Conclusion

Increased atrial pacing was the only predisposing factor of AHREs in Thai patients with permanent pacemaker. However, larger prospective study should be studied in the future.

Conflicts of interests

All authors have no any potential conflict of interest to disclose.

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