Atrial Size Independently Correlates with the Development of Paroxysmal Atrial Fibrillation in Patients with Sick Sinus Syndrome

Yu-Sheng Lin[1,3], MD; G. Bih-Fang Guo[2], MD; Yung-Lung Chen[2], MD; Tzu-Hsien Tsai[2], MD; Kuo-Li Pan[1,3], MD; Wen-Hao Liu[2], MD; Chien-Jen Chen[2], MD; Cheng-Hsu Yang[2], MD; Chih-Yuan Fang[2], MD; Yuan-Kai Hsieh[2], MD; Mien-Cheng Chen[2], MD

Background: Atrial fibrillation arises in 20-30% of patients with sick sinus syndrome, increasing the risk of systemic embolization and mortality. The aim of this study was to examine the clinical determinants of development of paroxysmal atrial fibrillation in sick sinus syndrome patients before implantation of a pacemaker.

Methods: This case-control survey involved 144 patients (mean age ± SD age: 72 ± 9 years) in whom implantation of a transvenous permanent pacemaker was planned for sick sinus syndrome. Patients were classified into two groups, patients with (n = 71) and without (n = 73) a history of paroxysmal atrial fibrillation before implantation. Clinical characteristics and echocardiographic parameters were analyzed.

Results: The peri-implant right atrial area and left atrial area were significantly larger in patients with, than those without, paroxysmal atrial fibrillation. Multiple logistic regression analysis identified that the size of the left atrial area independently correlated with the development of atrial fibrillation: each 1 cm^2 increase in left atrial area corresponded to a 44% increase in risk (odds ratio = 1.44 [1.22, 1.71]; $p < 0.001$).

Conclusions: The left atrial size independently correlates with the development of paroxysmal atrial fibrillation in sick sinus syndrome patients before pacemaker implantation.

(Chang Gung Med J 2010;33:659-67)

Key words: atrial fibrillation, atrial size, sick sinus syndrome

Sick sinus syndrome (SSS) is the most frequent indication for pacemaker implantation, and its incidence increases with age. Notably, 20~30% of patients with SSS have symptoms of paroxysmal or intermittent atrial fibrillation (AF),[1] and these patients may eventually develop chronic AF.[2-6] Atrial fibrillation is the most frequent sustained cardiac arrhythmia, contributing to increased risks of

From the [1]Division of Cardiology, Chang Gung Memorial Hospital at Chiayi, Chang Gung University Collage of Medicine, Taoyuan, Taiwan; [2]Division of Cardiology, Department of Internal Medicine, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Chang Gung University College of Medicine, Kaoshiung, Taiwan. [3]Chang Gung Institute of Technology, Taoyuan, Taiwan.
Received: Dec. 18, 2009; Accepted: Mar. 26, 2010
Correspondence to: Dr. Mien-Cheng Chen, Division of Cardiology, Department of Internal Medicine, Chang Gung Memorial Hospital-Kaohsiung Medical Center. 123, Dapi Rd., Niaosong Township, Kaohsiung County 833, Taiwan (R.O.C.)
Tel.: 886-7-7317123 ext. 8300; Fax: 886-7-7322402; E-mail: chenmien@ms76.hinet.net

systemic embolization and mortality.[5,7,8] However, clinical determinants of AF in patients with SSS are limited, mainly by invasive measurements after implantation.[9,10] Moreover, non-invasive clinical determinants of AF in patients with SSS before implantation are poorly defined. Atrial size has been reported to predict the development of AF in healthy individuals,[11] patients with nonrheumatic heart disease and patients with mitral valve disease following mitral valve surgery.[12-14] Accordingly, this study investigated the association of atrial size with the development of paroxysmal AF in SSS patients before implantation. Analytical results provided the scientific basis for further research to evaluate the diagnostic accuracy and predictive values of atrial size in predicting the development of AF in order to prevent thromboembolism and mortality related to AF in patients with SSS before implantation.

METHODS

Patient population

This case-control study surveyed 468 consecutive patients in whom implantation of a transvenous atrial-based or dual-chamber permanent pacemaker for SSS was planned in the accordance with the American College of Cardiology (ACC)/American Heart Association(AHA)/Heart rhythm Society (HRS) 2008 guidelines for device-based therapy of cardiac rhythm abnormalities.[15] Patients who did not receive transthoracic echocardiographic examinations within three months before or after the date of pacemaker implantation, or who did not receive electrophysiological study before implantation, were excluded (Fig. 1). Other exclusion criteria were hyperthyroidism, history of rheumatic heart disease, moderate or severe valve stenosis or regurgitation, valve repair or replacement, congenital heart disease, baseline abnormal ventricular wall motion related to ischemia, dilated cardiomyopathy and history of a previous myocardial infarction. Hence, the study population comprised 144 patients.

The SSS patients recruited for this study were classified into two groups, those with (n = 71) and without (n = 73) a history of paroxysmal AF before implantation. Paroxysmal AF was defined as episodic AF on an electrocardiogram, or transient AF (< 24 hours) on a 24-hour ambulatory electrocardiographic recording. Ischemic heart disease was defined if the patient had a coronary angiogram showing > 50% stenosis in any of the major coronary arteries or tested positive for myocardial ischemia on a thallium 201 scan or treadmill exercise test.

Electrophysiological study

Baseline electrophysiological data such as the PA interval, AH interval, HV interval, Wenckebach cycle length and corrected sinus nodal recovery time were measured.

Transthoracic echocardiography

Transthoracic echocardiographic examinations were performed by a 2.5-MHz transducer connected to a commercially available echo Doppler machine (Sonos 5500 or Sonos 7500; Hewlett-Packward; Palo Alto, CA, U.S.A.). The M-mode measurements were performed according to the recommendations of the American Society of Echocardiography.[16] The left and right atrial areas were measured by planimetry in a four-chamber view, and the maximum areas were the average of measurements (at the end of the T wave on the electrocardiogram) over two beats.[16] Echocardiographic data were collected on average four days before pacemaker implantation, i.e. –4.0 days (–17.0 day; 0.0 day) in SSS patients with paroxysmal AF and –4.0 days (–15.0 day; 1.0 day) in SSS patients without paroxysmal AF.

Statistical analysis

Continuous variables were described as mean ± SD. Categorical variables were presented as numbers or percentages. Continuous variables were compared with Student's t test (two-tailed) for parametric data and the Mann-Whitney U test for nonparametric data. Categorical variables were compared between the two groups by the chi-square test. The significance of multiple variables in univariate analysis was calculated by binary logistic regression analysis. To compare the predictive values of significant variables in logistic regression analysis, areas under the receiver operating characteristic (ROC) curve were constructed for sensitivity and specificity in predicting the development of paroxysmal AF. The best bound for predicting the development of AF was defined as that producing the highest sensitivity and specificity in distinguishing between SSS patients with and without paroxysmal AF. The ROC curve was adopted to calculate the best threshold. Sensitivity was

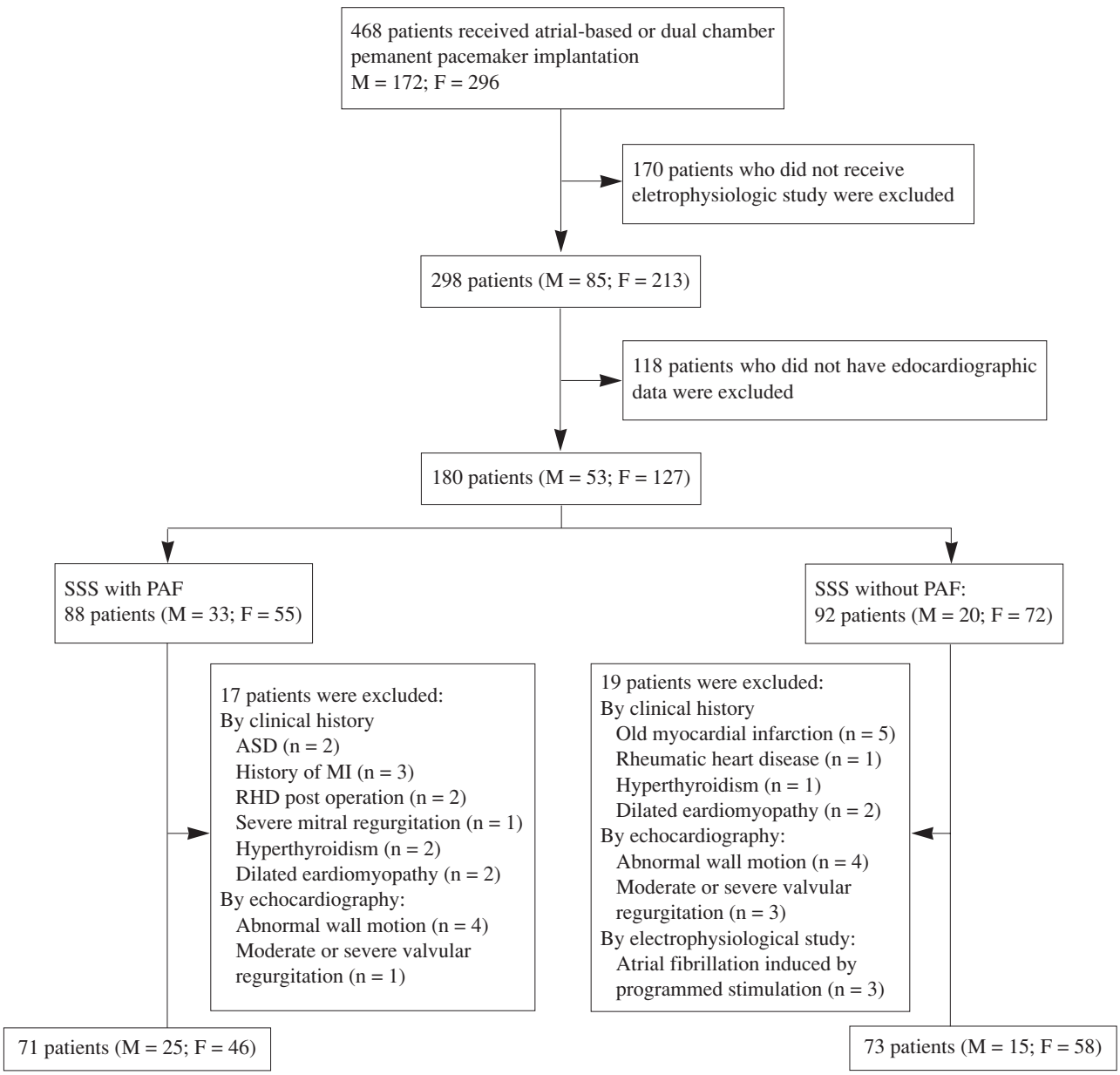

Fig. 1 Diagram of the case-control study. Abbreviations used: SSS: sick sinus syndrome; PAF: paroxysmal atrial fibrillation; ASD: atrial septal defect; MI: myocardial infarction; RHD: rheumatic heart disease.

defined as the proportion of SSS patients with paroxysmal AF whose predictor values were higher than the thresholds. Specificity was defined as the proportion of SSS patients without paroxysmal AF whose predictor values were lower than the thresholds. The positive predictive value was defined as the proportion of SSS patients with predictor values higher than the thresholds who had paroxysmal AF. The negative predictive value was defined as the proportion of SSS patients with the predictor values lower than the thresholds who did not have paroxysmal AF. Correlations were analyzed by Pearson's correlation. Statistical analysis was performed by SPSS 15 statistical software for Windows (SPSS Inc, Chicago, IL,

U.S.A.). All p values were two-sided, and the level of statistical significance was set at 0.05.

RESULTS

Baseline patient characteristics

Table 1 summarizes the clinical characteristics of the study patients. The two groups did not significantly differ in age, gender, body mass index, or body surface area, or in prevalence of diabetes mellitus, hypertension or ischemic heart disease. The two groups were balanced in terms of use of drugs such as angiotensin converting enzyme inhibitors and type I angiotensin II receptor blockers, β-blockers, Ca-blockers and statins.

Electrophysiological data

Table 2 summarizes the baseline electrophysiological data of the study patients. The two groups did not significantly differ in baseline sinus cycle lengths or intracardiac conduction times.

Correlation of atrial size with the development of paroxysmal AF before implantation

Table 3 lists the peri-implant echocardiographic data for patients with and without AF. No significant difference was observed between the two groups in terms of left ventricular ejection fraction. The right atrial area, left atrial area and left atrial diameter were significantly larger in SSS patients with than in those without paroxysmal AF. There was a significant correlation between the right atrial area and left atrial area ($r = 0.651$, $p < 0.001$). After adjustments for age, gender, body surface area, the presence of diabetes mellitus, hypertension and ischemic heart disease, use of β–blockers, Ca-blockers, and angiotensin converting enzyme inhibitors or type I angiotensin II receptor blockers, left ventricular dimension and left ventricular ejection fraction in multiple logistic regression analysis, the independent parameter correlated to the development of paroxysmal AF was the peri-implant left atrial area size, with an odds ratio for the development of paroxysmal AF of 1.44 for each 1-cm^2 increment in left atrial area (95% confidence interval, [1.22, 1.71], $p < 0.001$) (Table 4).

Discriminant analysis was performed to identify the peri-implant left atrial size as an independent parameter correlated to the development of paroxys-

Table 1. Baseline Clinical Characteristics of Patients

	SSS with paroxysmal AF ($n = 71$)	SSS without paroxysmal AF ($n = 73$)	p value
Age (years)	71.9 ± 9.1	72.1 ± 9.2	0.90
Men	25 (35.2%)	15 (20.5%)	0.06
BMI (kg/m^2)	24.4 ± 3.2	24.6 ± 4.1	0.77
BSA (m^2)	1.62 ± 0.16	1.57 ± 0.16	0.13
Diabetes mellitus	17 (23.9%)	18 (24.7%)	0.92
Hypertension	47 (66.2%)	44 (60.3%)	0.46
Ischemic heart disease	9 (12.7%)	15 (20.5%)	0.21
ACEI/ARB	24 (33.8%)	23 (31.5%)	0.77
β-blockers	17 (23.9%)	9 (12.3%)	0.07
Ca-blockers	25 (35.2%)	16 (21.9%)	0.08
Statins	5 (7.0%)	4 (5.5%)	0.74

Data are expressed as mean ± SD or number (%) of patients.

Abbreviations: AF: atrial fibrillation; ACEI/ARB: angiotensin converting enzyme inhibitor or type I angiotensin II receptor blocker; BMI: body mass index; BSA: body surface area; SSS: sick sinus syndrome.

Table 2. Electrophysiological Data

	SSS with paroxysmal AF ($n = 71$)	SSS without paroxysmal AF ($n = 73$)	p value
Basic sinus cycle length (msec)	988.0 ± 165.0	1054.0 ± 341.6	0.17
cSNRT (msec)	3807.0 ± 3359.8	5387.7 ± 5562.4	0.09
PR interval (msec)	181.2 ± 29.7	172.2 ± 28.0	0.14
PA (msec)	27.1 ± 9.5	32.1 ± 14.3	0.26
AH (msec)	104.7 ± 32.9	102.6 ± 36.9	0.74
HV (msec)	46.4 ± 9.5	45.8 ± 9.6	0.74
QRS (msec)	92.3 ± 20.3	90.1 ± 15.0	0.49
Antegrade Wenckebach cycle length (msec)	430.8 ± 102.7	429.6 ± 108.3	0.95

Data are expressed as mean ± SD.

Abbreviations: AF: atrial fibrillation; cSNRT: corrected sinus nodal recovery time; SSS: sick sinus syndrome.

Table 3. Baseline Echocardiographic Data

	SSS with paroxysmal AF (n = 71)	SSS without paroxysmal AF (n = 73)	p value
RA area (cm^2)	17.9 ± 4.2	15.2 ± 3.2	< 0.001
RA area index (cm^2/m^2)	11.0 ± 2.4	9.4 ± 1.7	< 0.001
LA area (cm^2)	26.3 ± 4.6	20.9 ± 3.6	< 0.001
LA area index (cm^2/m^2)	16.2 ± 3.1	13.1 ± 2.3	< 0.001
LA diameter (mm)	37.3 ± 5.5	33.4 ± 4.6	< 0.001
LA diameter index (mm/m^2)	22.8 ± 3.6	21.4 ± 3.7	0.048
LVEF (%)	70.5 ± 8.6	71.3 ± 7.3	0.508

Abbreviations: AF: atrial fibrillation; LA: left atria; LVEF: left ventricular ejection fraction; RA: right atria; SSS: sick sinus syndrome.
RA and LA area index: RA and LA area divided by body surface area; LA diameter index: LA diameter divided by body surface area.

Table 4. Multiple Logistic Regression Analysis of Clinical and Echocardiographic Parameters Relevant to the Development of Paroxysmal Atrial Fibrillation in Sick Sinus Syndrome Patients before Implantation

Variables	Odds ratio	95% Confidence interval	p value
Left atrial area (cm^2)	1.44	1.22-1.71	< 0.001
Left atrial area index	1.78	1.36-2.33	< 0.001

mal AF. The area under the ROC curve for a cut-off value of 24.1 cm^2 for the left atrial area was 0.82 (95% confidence interval, [0.74, 0.89]) (Fig. 2). The sensitivity and specificity of a threshold of 24.1 cm^2 for the left atrial area were 68.3% (95% confidence interval, [0.55, 0.79]) and 80.0% (95% confidence interval, [0.67, 0.89]), respectively, while the positive and negative predictive values were 77.4% (95% confidence interval, [0.63, 0.87]) and 71.6% (95% confidence interval, [0.59, 0.82]), respectively. The incidence of development of paroxysmal AF was significantly greater in patients with a peri-implant left atrial area > 24.1 cm^2 than in patients with a left atrial area < 24.1 cm2 (odds ratio: 8.63, 95% confidence interval, [3.75, 19.88], $p < 0.001$).

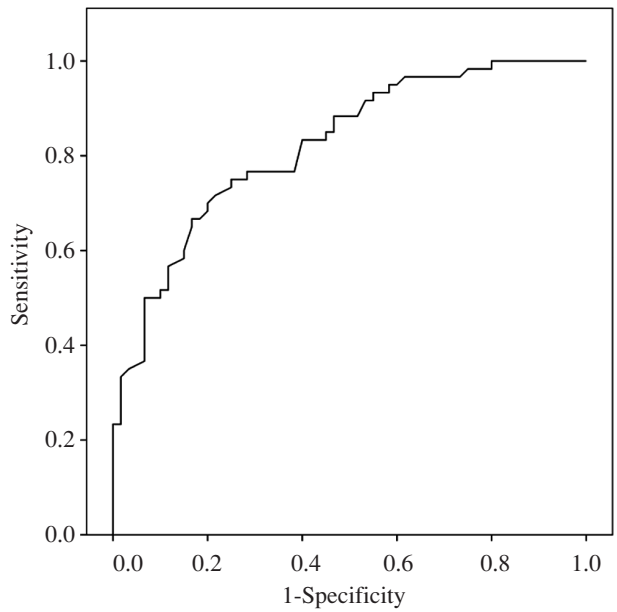

Fig. 2 The area under the receiver operating characteristic curve for a cut-off value of 24.1 cm^2 for the left atrial area was 0.82 (95% confidence interval, [0.74, 0.89]).

DISCUSSION

This study examined the clinical determinants of development of paroxysmal AF in patients with SSS prior to implantation. Several important conclusions were drawn from this study. The size of the peri-implant left atrial area independently correlated with the development of AF in SSS patients: each 1 cm^2 increase in left atrial area corresponded to a 44% increase in risk for the development of paroxysmal AF. The risk for development of paroxysmal AF in SSS patients was 8.6-fold when the left atrial area was > 24.1 cm^2. Thus, this study found that the left atrial size was a clinical determinant of development of paroxysmal AF in SSS patients prior to pacemaker implantation.

Atrial fibrillation, the most common sustained cardiac arrhythmia, is frequently caused by micro-reentry circuits of electrical impulses in the atrial wall, a process called the multiple-wavelets mechanism. The incidence of wavelets that can coexist is determined by both the mass and the electrical vul-

nerability of the atrial myocardium, which explains why AF is frequently seen in clinical situations linked with enlargement of the atrium and shortening of the atrial refractory period.[13,14,17-19] Sick sinus syndrome is an age-related degenerative process of the sinus node, characterized by fibrosis, ischemia, and fatty infiltration or destruction of the sinus node itself, or destruction of the sinoatrial area resulting from ischemia, inflammation or degenerative changes in the nerves and ganglia surrounding the sinus node or pathological changes in the atrial myocardial wall.[2,3] All of these factors lead to reduced automaticity of the sinus node, decreased sinoatrial conduction velocity, prolonged intra-atrial and interatrial conduction, local and regional conduction delay, increased dispersion of refractoriness and even ectopic atrial automaticity, and thus to the development of AF.[20-22] Therefore, AF develops in the natural history of SSS.[1]

Many studies have adopted invasive measurements to indicate differences in atrial electrophysiological characteristics. These measurements have been adopted to differentiate or predict the risk of development of AF in SSS, including the distribution of abnormal atriograms under right atrium mapping,[23] fragmentation of atrial activity elicited by premature stimulation and the vulnerability index.[9,10,24] Although these parameters seem to successfully differentiate patients with AF from those without it, they require invasive measurement and are not practical in clinical practice. Prolongation of the P-wave or P-wave dispersion has been adopted to predict AF following ventricular-based pacemaker implantation.[25] The hypothesis is that sinus node disease prolongs intra-atrial or interatrial conduction time, and leads to abnormalities in the morphology and the duration of the P wave on a 12-lead surface electrocardiogram.[26,27] A previous study reported that a threshold of 110 ms for the duration of the P-wave had good diagnostic accuracy for predicting the development of AF.[26] However, a difference of several milli-seconds in a clinical scenario is difficult to differentiate accurately. The P wave characteristics derived from surface electrocardiograms have been indicated to correlate well with echocardiographic measurements.[28-31] The atrial size has been adopted to predict the risk of mortality, thromboembolism and the development of AF in paced patients with SSS.[32] However, the differentiating value of atrial size for paroxysmal AF in SSS patients before implantation has never been studied. This study provides non-invasive echocardiographic measurements and specific cutoff values for atrial size, thus successfully differentiating SSS patients with and without paroxysmal AF. Additionally, the normal size of the left atrial area is ≤ 20 cm^2.[16,33] The left atria of SSS patients with paroxysmal AF in this study were larger than those of the healthy population (Table 3).

Study limitations

The potential limitations of this study relate mainly to its retrospective nature. First, this study adopted peri-implant transthoracic echocardiographic measurements. However, Suarez et al. indicated that left atrial size in patients with paroxysmal AF increased slowly during follow-up, by 10.8% over 6.2 years.[34] Liu et al. reported no change in left atrial size in patients with lone paroxysmal AF 3 months after beginning anti-arrhythmic therapy.[35] Therefore, the change in atrial size within the three months before and after pacemaker implantation would be expected to be small. Second, inter-observer variations from several echocardiographers who performed the echocardiographic studies were not assessed due to the retrospective nature of this study. Third, this retrospective study intended to find clinical parameters associated with the development paroxysmal AF in sick sinus syndrome patients before pacemaker implantation. Therefore, it did not provide data related to the development of AF in patients who did not have sick sinus syndrome. Fourth, follow-up data were not specifically examined in this retrospective study. Therefore, correlation of the presence of peri-implant paroxysmal AF and the subsequent development of AF after implantation could not be assessed in this study. Finally, the possibility of the existence of asymptomatic paroxysmal AF in those SSS patients defined as not having paroxysmal AF based on surface electrocardiograms or 24-hour ambulatory electrocardiographic recordings could not be entirely excluded.

Clinical implications

Future large, prospective studies should determine the diagnostic accuracy and predictive values of atrial size in predicting the development of AF. This would help clincians predict AF and take action earlier to avert the risks of thromboembolism and

mortality related to AF in patients with SSS before implantation.

Conclusion

Left atrial size independently correlates with the development of paroxysmal AF in SSS patients before pacemaker implantation.

REFERENCES

1. Sutton R, Kenny RA. The natural history of sick sinus syndrome. Pacing Clin Electrophysiol 1986;9:1110-4.
2. Alpert MA, Flaker GC. Arrhythmias associated with sinus node dysfunction: Pathogenesis, recognition, and management. JAMA 1983;250:2160-6.
3. Ferrer MI. The sick sinus syndrome in atrial disease. JAMA 1968;206:645-6.
4. Lamas GA, Lee KL, Sweeney MO, Silverman R, Leon A, Yee R, Marinchak RA, Flaker G, Schron E, Orav EJ, Hellkamp AS, Greer S, McAnulty J, Ellenbogen K, Ehlert F, Freedman RA, Estes NA 3rd, Greenspon A, Goldman L. Ventricular pacing or dual chamber pacing for sinus node dysfunction. N Engl Med 2002;346:1854-62.
5. Sgarbossa EB, Pinski SL, Maloney JD, Simmons TW, Wilkoff BL, Castle LW, Trohman RG. Chronic atrial fibrillation and stroke in paced patients with sick sinus syndrome. Circulation 1993;88:1045-53.
6. Skanes AC, Krahn AD, Yee R, Klein GJ, Connolly SJ, Kerr CR, Gent M, Thorpe KE, Roberts RS. Canadian Trial of Physiologic Pacing. Canadian Trial of Physiologic Pacing: Progression to chronic atrial fibrillation after pacing. J Am Coll Cardiol 2001;38:167-72.
7. Chesebro JH, Fuster V, Halperin JL. Atrial fibrillation - risk marker for stroke. N Engl J Med 1990;323:1556-8.
8. Benjamin EJ, Wolf PA, D'Agostino RB, Silbershatz H, Kannel WB, Levy D. Impact of atrial fibrillation on the risk of death: the Framingham heart study. Circulation 1998;98:946-52.
9. De Sisti A, Leclercq JF, Fiorello P, Di Lorenzo M, Manot S, Halimi F, Attuel P. Sick sinus syndrome with and without atrial fibrillation: atrial refractoriness and conduction characteristics. Cardiologia 1999;44:361-7.
10. De Sisti A, Attuel P, Manot S, Fiorello P, Halimi F, Leclercq JF. Electrophysiological characteristics of the atrium in sinus node dysfunction with and without postpacing atrial fibrillation. Pacing Clin Electrophysiol 2000;23:303-8.
11. Mont L, Tamborero D, Elosua R, Molina I, Coll-Vinent B, Sitges M, Vidal B, Scalise A, Tejeira A, Berruezo A, Brugada J. Physical activity, height, and left atrial size are independent risk factors for lone atrial fibrillation in middle-aged healthy individuals. Europace 2008;10:15-20.
12. Vaziri SM, Larson MG, Benjamin EJ, Levy D. Echocardiographic predictors of nonrheumatic atrial fibrillation. The Framingham Heart Study. Circulation 1994;89:724-30.
13. Chen MC, Chang JP, Guo GBF, Chang HW. Atrial size reduction as a predictor of the success of radiofrequency maze procedure for chronic atrial fibrillation in patients undergoing concomitant valvular surgery. J Cardiovasc Electrophysiol 2001;12:867-74.
14. Chen MC, Chang JP, Chang HW, Chen CJ, Yang CH, Chen YH, Fu M. Clinical determinants of sinus conversion by radiofrequency maze procedure for persistent atrial fibrillation in patients undergoing concomitant mitral valvular surgery. Am J Cardiol 2005;96:1553-7.
15. Epstein AE, DiMarco JP, Ellenbogen KA, Estes NA 3rd, Freedman RA, Gettes LS, Gillinov AM, Gregoratos G, Hammill SC, Hayes DL, Hlatky MA, Newby LK, Page RL, Schoenfeld MH, Silka MJ, Stevenson LW, Sweeney MO, Smith SC Jr, Jacobs AK, Adams CD, Anderson JL, Buller CE, Creager MA, Ettinger SM, Faxon DP, Halperin JL, Hiratzka LF, Hunt SA, Krumholz HM, Kushner FG, Lytle BW, Nishimura RA, Ornato JP, Page RL, Riegel B, Tarkington LG, Yancy CW. ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 2008;117:e350-408.
16. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise JS, Solomon SD, Spencer KT, Sutton MS, Stewart WJ. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr. 2005;18:1440-63.
17. Henry WL, Morganroth J, Pearlman AS, Clark CE, Redwood DR, Itscoitz SB, Epstein SE. Relation between echocardiographically determined left atrial size and atrial fibrillation. Circulation 1976;53:273-9.
18. Rensma PL, Allessie MA, Lammers WJ, Bonke FI, Schalij MJ. Length of excitation wave and susceptibility to reentrant atrial arrhythmias in normal conscious dogs. Circ Res 1988;62:395-410.
19. Wijffels MC, Kirchhof CJ, Dorland R, Allessie MA. Atrial fibrillation begets atrial fibrillation. Circulation 1995;92:1954-8.
20. Misier AR, Opthof T, van Hemel NM, Defauw JJ, de Bakker JM, Janse MJ, van Capelle FJ. Increased dispersion of "refractoriness" in patients with idiopathic paroxysmal atrial fibrillation. J Am Coll Cardiol 1992;19:1531-5.
21. Cosio FG, Palacios J, Vidal JM, Cocina EG, Gómez-Sánchez MA, Tamargo L. Electrophysiologic studies in atrial fibrillation: slow conduction of premature impulses,

a possible manifestation of the background for reentry. Am J Cardiol 1983;51:122-30.
22. Buxton AE, Waxman HL, Marchlinski FE, Josephson ME. Atrial conduction: effect of extrastimuli with or without atrial dysrhythmias. Am J Cardiol 1984;54:755-61.
23. Centurion OA, Fukatani M, Konoe A, Tanigawa M, Shimizu A, Isomoto S, Kaibara M, Hashiba K. Different distribution of abnormal endocardial electrograms within the right atrium in patients with sick sinus syndrome. Br Heart J 1992;68:596-600.
24. Tanigawa M, Fukatani M, Konoe A, Isomoto S, Kadena M, Hashiba K. Prolonged and fractionated atrial electrograms during sinus rhythm in patients with paroxysmal atrial fibrillation and sick sinus node syndrome. J Am Coll Cardiol 1991;17:403-8.
25. Snoeck J, Decoster H, Vrints C, Marchand X, Kahn JC, Verherstraeten M, Berkhof M, Franque L. Predictive value of the P wave at implantation for atrial fibrillation after VVI pacemaker implantation. Pacing Clin Electrophysiol 1992;15:2077-83.
26. Liu Z, Hayano M, Hirata T, Tsukahara K, Quin Y, Nakao K, Nonaka M, Ishimatsu T, Ueyama C, Yano K. Abnormalities of electrocardiographic P wave morphology and their relation to electrophysiological parameters of the atrium in patients with sick sinus syndrome. Pacing Clin Electrophysiol 1998;21:79-86.
27. Snoeck J, Decoster H, Verherstraeten M, Berkhof M, Vorlat A, Heuten H, Vrints C, Kahn JC, Marchand X. Evolution of P wave characteristics after pacemaker implantation. Pacing Clin Electrophysiol 1990;13:2091-5.
28. Ariyarajah V, Prajapat L, Kumar KK, Barac I, Apiyasawat S, Spodick DH. Quantitative estimation of left atrial linear dimension on a transthoracic echocardiogram using an electrocardiographic formulaic assessment. Am J Cardiol 2007;100:894-8.
29. Birkbeck JP, Wilson DB, Hall MA, Meyers DG. P-wave morphology correlation with left atrial volumes assessed by 2-dimensional echocardiography. J Electrocardiol 2006;39:225-9.
30. Jose VJ, Krishnaswami S, Prasad NK, Rath PC, Kothari SS. Electrocardiographic left atrial enlargement--correlation with echo. J Assoc Physicians India 1989;37:497-9.
31. Hazen MS, Marwick TH, Underwood DA. Diagnostic accuracy of the resting electrocardiogram in detection and estimation of left atrial enlargement: an echocardiographic correlation in 551 patients. Am Heart J 1991;122:823-8.
32. Mattioli AV, Tarabini Castellani E, Mattioli G. Stroke in paced patients with sick sinus syndrome: influence of left atrial function and size. Cardiology 1999;91:150-5.
33. Hagan AD, DiSessa TG, Bloor CM, Calleja HB. Two-dimensional Echocardiography: Clinicial-pathological Correlations in Adults and Congenital Heart Disease. Boston: Little Brown, 1983:553.
34. Suarez GS, Lampert S, Ravid S, Lown B. Changes in left atrial size in patients with lone atrial fibrillation. Clin Cardiol 1991;14:652-6.
35. Liu Z, Ling Z, Su L, Wu J, Lan X, Chen Y, Du H, She Q, Yin Y. The effect of different treatment strategies on left atrial size in patients with lone paroxysmal atrial fibrillation-a prospective cohort study. J Interv Card Electrophysiol 2008;23:167-73.

心房大小的變化在病竇症候群病人中是否發展成心房顫動有獨立的相關性

林祐賸[1,3] 郭必芳[2] 陳永隆[2] 蔡子賢[2] 潘國利[1,3] 劉文浩[2] 陳建仁[2]
楊正旭[2] 方志元[2] 謝元凱[2] 陳勉成[2]

背 景： 在病竇症候群病人當中，具有心房顫動的病人約佔 20-30%。且在這類病人當中，也因爲具有心房顫動而增加了全身性栓塞及死亡的風險。因而這研究目的旨在探討病人尚未置入節律器之前，是否有決定性的因子可以事前預知病人是否有較高發生心房顫動的機會。

方 法： 此案例控制研究包括了 144 位預計要置入節律器的病竇症候群病人 (平均年齡±標準偏差：72 ± 9 歲)。將這些病人分爲兩群：一爲在置入節律器之前即具有陣發性心房顫動的病人 (71 人)；一爲在置入節律器之前不具有陣發性心房顫動的病人 (73 人) 。進而在這兩組人中探討臨床上的特徵及心臟超音波的參數有何差異。

結 果： 在置入節律器前時所做的心臟超音波顯示：不論左心房或右心房，在置入節律器之前即具有陣發性心房顫動的病人都會比不具有陣發性心房顫動的病人來得大。將這些臨床及超音波參數進行多因子變異數分析後可以發現：心房大小的變化和發展心房顫動的機會有獨立的相關性。在左心房每增大 1 平方公分即可增加發生心房顫動 44% 的風險 (Odds ratio = 1.44 [1.22, 1.71]; $p < 0.001$)

結 論： 左心房在病竇症候群病人於置入節律器之前的大小，對於預測病人是否會發生陣發性心房顫動的機會是一個不錯的指標。

(長庚醫誌 2010;33:659-67)

關鍵詞：心房顫動，心房大小，病竇症候群

[1]長庚醫療財團法人嘉義長庚紀念醫院 內科部 心臟內科；[2]長庚醫療財團法人高雄長庚紀念醫院 內科部 心臟內科；長庚大學 醫學院；[3]長庚技術學院
受文日期：民國98年12月18日；接受刊載：民國99年3月26日
通訊作者：陳勉成醫師，長庚醫療財團法人高雄長庚紀念醫院 內科部 心臟內科。高雄縣833鳥松鄉大埤路 123 號。
Tel.: (07)7317123轉8300; Fax: (07)7322402; E-mail: chenmien@ms76.hinet.net