Gender Differences of Electrophysiological Characteristics in Focal Atrial Tachycardia

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Gender differences of supraventricular tachycardias such as atrioventricular nodal re-entry, atrioventricular re-entry, and atrial fibrillation have been reported. There is little evidence of the effect of gender on focal atrial tachycardia (FAT). The study consisted of 298 patients who were referred to this institution for radiofrequency catheter ablation of FAT from October 1992 to April 2008 and included 156 men (52%) and 142 women (48%). Men were significantly older than women (57.9 ± 18.2 vs 47.2 ± 19.0 years old, p <0.001). Women had more associated arrhythmias (17.0% vs 28.9%, p = 0.01), mostly due to an increased incidence of atrioventricular nodal re-entrant tachycardia. Men had more cardiovascular co-morbidities (19.9% vs 9.9%, p = 0.02), a mechanism of increased automaticity (19.1% vs 8.1%, p = 0.01), and nonparoxysmal tachycardia (14.7% vs 4.4%, p = 0.01). No gender differences were noted among FAT number, left atrial involvement, shortest tachycardia cycle, success rate of catheter ablation, or recurrence rate of FAT. Mean duration of follow-up was 63.2 ± 47.5 months. Premenopausal women had a lesser cardiovascular co-morbidity (15.3% vs 4.3%, p = 0.04) and a greater incidence of a mechanism of increased automaticity (13.4% vs 2.9%, p = 0.03). In conclusion, gender differences in electrophysiologic characteristics were noted in FAT. **(Am J Cardiol 2009;104:97–100)**

It is becoming increasingly apparent that there are important gender differences in normal cardiac physiology. These in turn could be associated with differences in type and severity of cardiac arrhythmias. Baseline QT interval has been found to be longer in women than in men.[1] Incidence of torsade de pointes associated with medications appears higher in women.[2] Atrioventricular nodal re-entrant tachycardia (AVNRT) has been demonstrated to have a 2:1 female preponderance. Women have shorter slow pathway refractory periods, atrioventricular block cycle lengths, and tachycardia cycle lengths.[3] In atrial fibrillation, female gender could predict the presence of SVC ectopic beats.[4] There is little evidence for the effect of gender on other, less common, types of supraventricular tachycardias such as focal atrial tachycardia (FAT). In this report, we review a series of patients referred for catheter ablation of FAT and compared gender differences of electrophysiologic characteristics.

Methods

The study consisted of 298 patients who were referred to this institution for an electrophysiologic study and radiofrequency catheter ablation of FAT from October 1992 to April 2008. Patients were 15 to 96 years old.

Informed written consent was obtained from all patients. As described previously, patients were studied in the postabsorptive, nonsedated state.[5] All antiarrhythmic drugs were discontinued for ≥5 1/2-lives before the study. A 7Fr, deflectable, decapolar catheter with a 2-mm interelectrode distance and 5-mm spacing between each electrode pair was also inserted into the coronary sinus through the internal jugular vein. The position of the proximal electrode pair at the ostium of the coronary sinus was confirmed with a contrast injection. A 9Fr sheath placed in the right femoral vein was used to introduce the ablation catheter. Three multipolar, deflectable-tip, closely spaced (2 mm) electrode catheters were positioned in the right atrium, His-bundle area, and right ventricle through the femoral vein. Rapid right atrial stimulation (using pacing cycle lengths from 600 ms until 2:1 capture was noted) and right atrial extrastimuli (single or double) were used for the induction and termination of FAT, and these were repeated 2 to 4 times to ensure reproducibility of responses. If programmed electrical stim-

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Table 1
Comparisons of general characteristics between men and women

Variable	Men (n = 156)	Woman (n = 142)	p Value
Age (yrs)	57.9 ± 18.2	47.2 ± 19.0	<0.001
Cardiovascular co-morbidity	19.9%	9.9%	0.02
Congenital heart disease	2.6%	2.8%	
Diabetes mellitus	0.6%	0.7%	
Hypertension	7.1%	4.2%	
Dilated cardiomyopathy	3.8%	1.4%	
Hypertrophic cardiomyopathy	0.6%	0	
Coronary heart disease	5.8%	0.7%	
Valvular heart disease	1.3%	0.7%	
Cor pulmonale	0.6%	0	
Associated arrhythmia	17.3%	28.9%	0.01
AVNRT	5.1%	12.7%	
Atrial flutter/fibrillation	9.6%	10.5%	
Atrioventricular re-entrant tachycardia	3.2%	1.4%	

Table 2
Differences between electrophysiologic parameters

Variable	Men	Women	p Value
Spontaneous cycle length	753 ± 161	730 ± 145	0.39
Atriohisian interval	92 ± 29	97 ± 77	0.78
Hisian–ventricular interval	42 ± 47	41 ± 7	0.50
AVN ERP	303 ± 45	298 ± 53	0.41
AVN FRP	397 ± 51	399 ± 64	0.99
Atrial ERP	216 ± 29	216 ± 36	0.91
Atrial FRP	242 ± 33	242 ± 37	0.91
Ventricular ERP	219 ± 25	227 ± 27	0.18
Ventricular FRP	241 ± 29	249 ± 6	0.21

ulation failed to induce FAT, isoproterenol (at graded dosages from 1 to 4 μg/min) was infused intravenously until FAT developed or sinus rate increased to 20% above the value at rest. An intravenous bolus of adenosine (3 to 18 mg) was given to observe the effects of adenosine on terminating FAT. Electrophysiologic criteria used for diagnosis of focal FAT have been reported.[5,6]

Catheter ablation (40 to 50 W, 50°C to 60°C, 40 seconds) was performed using a 4-mm, electrode-tipped, nonirrigated ablation catheter connected to an EPT-1000 generator (Boston Scientific Co., Natick, Massachusetts). We delivered radiofrequency energy to the FAT origin. When a left-sided origin was suspected, a trans-septal puncture was performed. Conventional endocardial mapping studies and catheter ablation were performed the same as in the right atrium. After catheter ablation, the same stimulation protocol as that used to induce the FAT before ablation was performed to ensure that FAT was noninducible. Successful catheter ablation was defined as the inability to reinduce FAT. After discharge from the hospital, patients were followed-up closely in the outpatient clinic. Long-term efficacy was assessed clinically by surface electrocardiogram at rest, 24-hour Holter monitoring, event recorder for a 1-week recording duration, and clinical symptoms.

Automatic FAT was defined as a tachycardia that could not be initiated or terminated by programmed electrical stimulation; the other tachycardias were defined as nonautomatic

Table 3
Comparisons of electrophysiologic characteristics between men and women

Variable	Men	Women	p Value
FAT no.	1.2 ± 0.5	1.2 ± 0.6	0.78
Left atrial focus	13.2%	15.4%	0.61
Increased automaticity	19.1%	8.1%	0.01
Nonparoxysmal tachycardia	14.7%	4.4%	0.01
Shortest cycle length (ms)	364 ± 88	368 ± 65	0.68
Successful ablation	92.6%	94.6%	0.62

Table 4
Comparisons of electrophysiologic characteristics between menopausal and premenopausal women

Variable	Menopausal Women (n = 73)	Premenopausal Women (n = 69)	p Value
Cardiovascular co-morbidity	15.3%	4.3%	0.04
Associated arrhythmia	30.1%	27.5%	0.85
FAT no.	1.2 ± 0.5	1.2 ± 0.6	0.78
Left atrial focus	19.7%	10.8%	0.16
Increased automaticity	2.9%	13.4%	0.03
Nonparoxysmal tachycardia	5.7%	3.0%	0.73
Shortest cycle length (ms)	374 ± 66	363 ± 66	0.41
Successful ablation	94.2%	95.1%	0.99

FATs. Nonparoxysmal tachycardia included chronic, continuous, persistent, and incessant tachycardia. Other tachycardias were defined as paroxysmal tachycardia. Associated arrhythmias were defined as arrhythmias that differed from FAT by electrophysiologic criteria and clinical judgment. We divided the right atrium into 7 areas: atrial septum, right atrial appendage, ostium of the superior vena cava, tricuspid annulus, ostium and body of the coronary sinus, and an area that did not belong to the other areas and was defined as the right atrial free wall. The entire left atrium was considered a single area.

Continuous data were expressed as mean ± SD. Comparisons of parametric data were performed using Student's *t* test, and comparisons of nonparametric data were performed using chi-square test with Yates correction or Fisher's exact test.

Results

Men were significantly older than women. Men had more cardiovascular co-morbidities (Table 1). The most common cardiovascular disease in men and women was hypertension. Prevalence of associated arrhythmias was higher in women than in men. The most common associated arrhythmia in men was atrial flutter/fibrillation, and that in women was AVNRT. Prevalence of associated AVNRT showed a 2:1 predominance in women, but prevalence of atrial flutter/fibrillation was similar. Common locations of FAT in men and women were from the right free wall and those that followed were from the right atrial septum or left atrium.

Baseline electrophysiological parameters (Table 2) exhibited no gender differences between the spontaneous cy-

cle length, atriohisian interval, hisian–ventricular interval, AVN effective refractory period (ERP), AVN functional effective refractory period (FRP), atrial ERP, atrial FRP, ventricular ERP, or ventricular FRP.

Men had more FAT due to increased automaticity (Table 3) and nonparoxysmal tachycardia. No gender difference was noted among FAT number, left atrial involvement, shortest tachycardia cycle, and success rate of catheter ablation. Mean duration of follow-up was 63.2 ± 47.5 months. There were no gender differences between recurrence rates of FAT.

Women were further divided into 2 groups. One was menopausal, and the other was premenopausal. Premenopausal women had fewer cardiovascular co-morbidities (Table 4), but a greater incidence of a mechanism of increased automaticity than menopausal women. Associated arrhythmias, FAT number, left atrial involvement, nonparoxysmal tachycardia, shortest cycle, and success rate of catheter ablation exhibited no differences.

Discussion

To the best of our knowledge, this was the largest current cohort study describing different electrophysiologic characteristics of FAT between men and women. Women had more associated arrhythmias, especially AVNRT. Prevalence of FAT increased with age in men. Men had more FATs with an increased automaticity mechanism, nonparoxysmal tachycardia, and cardiovascular co-morbidities. Menopausal women had less FAT due to increased automaticity and greater cardiovascular co-morbidities compared with premenopausal women.

Liu et al[7] investigated age- and gender-related atrial electrophysiologic and structural changes. No significant difference in atrial ERP was found between women and men. However, women did have significantly longer ventricular ERPs compared with men. In the present study, similarly, no differences in atrial ERPs between women and men were noted. However, no differences in ventricular ERPs were noted.

Maurer et al[8] investigated the prevalence of exercise-induced supraventricular tachycardias in a population of healthy volunteers, in which approximately 2/3 of episodes of >10 beats in length favored an ectopic atrial origin. Prevalence of supraventricular tachycardia increased with age in men but not in women. Liu et al[7] reported that left atrial dimension was greater in elderly patients and men, which implied a diseased atrium and promotion of arrhythmogenesis. Those reports explained why men with FAT were older than women in the present study. In the present study, men were also reported to have more cardiovascular co-morbidities and a higher incidence of nonparoxysmal tachycardia.

Mechanisms of arrhythmias due to increased automaticity, e.g., inappropriate sinus tachycardia and accelerated junctional rhythm, have been suggested to be due to increased sympathetic activity.[9,10] Men had a higher sympathetic output than women.[11] Therefore, men may have a higher incidence of FAT due to increased automaticity than women, which implies possible regulation of the autonomic nervous system and sex hormones in the pathogenesis of FAT.

In premenopausal women, more FATs due to increased automaticity were noted. Further comparisons between premenopausal and menopausal women showed that the incidence of FAT due to increased automaticity in premenopausal women was higher than that in menopausal women. There are 2 possible mechanisms. First, more cardiovascular co-morbidities might imply greater diffuse atriopathy, enlarged atrium, and complex atrial arrythmias.[12,13] A diseased atrium with interstitial fibrosis also promotes arrhythmogenesis due to nonautomatic mechanisms such as re-entry or triggered activity by interfering with atrial conduction properties.[14,15] Premenopausal women have fewer cardiovascular co-morbidities and therefore fewer FATs. Another explanation was the possibility of it being related to sex hormones. Progesterone has been reported to increase attacks of SVT, which was due to a direct hormonal effect or partly through an increased sympathetic output caused by progesterone.[16] Premenopausal women had a higher serum level of progesterone. Therefore, more FATs with increased automaticity were noted in premenopausal women than menopausal women.

This is a retrospective cohort study from a tertiary referral center, and the age difference between men and women could be in part a referral bias, which complicates the attribution of these co-morbidities. Roles of hormone replacement therapy and oral contraceptive use were not analyzed in the present study. Also, relations among FAT attacks, timing of electrophysiologic study, and phase of menstrual cycle were not analyzed. In future studies, a larger population from different centers and with more delicate designs regarding menstrual cycle will be necessary.

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