Focal atrial tachycardia-the localization differences between men and women: A study of 487 consecutive patients

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Abstract

Objective: The preferential sites for focal atrial tachycardia (FAT) are mainly in the right atrium in both sexes. However, a limited number of studies have indicated that sex differences in the localization of FAT. This study investigated possible sex differences in the distribution of FAT in a large cohort of patients referred for ablation.

Methods: From 2004 to 2019, 487 patients (298 women) were referred to our institution for ablation of FAT. A standard electrophysiological study was conducted, and isoproterenol or atropine was given when needed. Conventional catheter mapping, electroanatomic contact mapping, and noncontact mapping were used to assess the origin of ectopic atrial tachycardia.

Results: Overall, 451 foci were successfully ablated in 436 patients (90%). Although the foci located along the crista terminalis were more common in women than in men (42% vs. 29%; p=0.023), the opposite were found in the foci located along the tricuspid annulus (5% vs. 11%; p=0.032) and the right atrial appendage (RAA) (1% vs. 3%; p=0.032). Other locations were similarly distributed in men and women. In addition, the presence of persistent FAT was more frequent in men than in women (22% vs. 5%; p<0.001). Finally, the difference in the induction pattern of FAT was also remarkable between sexes.

Conclusion: The distribution of FAT in women and men is different. In addition, persistent FAT seems more often in men than in women. The different distribution, persistency, and induction pattern of FAT should be considered in the successful management of this type of tachycardia. *(Anatol J Cardiol 2020; 24: 405-9)*

Keywords: focal atrial tachycardia, localization, persistent, sexes, ablation

Introduction

Atrial tachycardias (ATs) excluding atrial fibrillation (AF) and cavotricuspid isthmus-dependent atrial flutter (AFL) account for 10% of supraventricular tachycardias referred for ablation procedure. More than 70% of these cases are focal and occur in patients with no records of cardiac surgery or ablation of AF. In most ablation reports, focal atrial tachycardia (FAT) is more common in women than in men (1-3). The ablation success rate seems to be as equal in women and men (4).

The preferential sites for FAT in the right atrium are crista terminalis (CT), coronary sinus ostium (CS os), inferior septal region, and along the tricuspid annulus (TA). In addition, pulmonary veins (PVs) and mitral annulus are the more encountered regions in the left atrium (5). There are a limited number of studies with a small number of patients, which suggest sex differences in localization, persistency, and mechanism of FATs (4, 6, 7). This study aimed to reveal the possible sex differences in the distribution of FATs in a large cohort of patients who were referred for ablation procedure.

Methods

Patients

From 2004 to 2019, 487 patients [189 men with a mean age of 53 years (range, 14–85) and 298 women with a mean age of 52 years (range, 14–88)] were referred to our institution for ablation of focal AT. Patients with AT after cardiac surgery or catheter ablation, which previous lesions might constitute a substrate for the AT (i.e., all left-sided ATs with previous AF ablation, posterior or posteroseptal ATs in patients with previous isthmus ablation),

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were excluded. Demographic and clinical data were collected before the ablation procedure (Table 1). The study was approved by the Institutional Ethics Committee.

Electrophysiological study and ablation procedure

At least 5 half-lives of antiarrhythmic medications were discontinued before the procedure. All procedures were performed in a light sedation and in the fasting state. A standard electrophysiological study was conducted by programmed electrical stimulation and burst pacing from the CS or high right atrium in the absence of spontaneous tachycardia, and isoproterenol or atropine was given when needed to induce tachycardia.

Focal AT was defined as the activation with a centrifugal pattern from a single focus and with an isoelectric interval between P waves on the surface ECG. The AT origin was assessed by conventional catheter mapping (n=324), electroanatomic contact mapping (n=137) (Carto, Biosense Webster, Inc., Diamond Bar, CA, USA; EnSite NavX™, St. Jude Medical, Inc., St. Paul, MN, USA), or noncontact mapping (n=63) (EnSite NavX™, St. Jude Medical, Inc., St. Paul, MN, USA). The tachycardias from the posteroseptal region and CS os classified were together because of their close anatomic correlations. Because of our ablation experience with focal cryocatheter and owing to the safety reasons, in 197 patients (121 women and 76 men), we have preferred focal cryoablation catheter for tachycardias that particularly originated from anteroseptal part, midseptal part, upper part of the CT, and septal part of the tricuspid valve to avoid damage of the sinoatrial node, phrenic nerve, and atrioventricular (AV) node. Successfully treated foci and failed foci in which ablation had been aborted owing to the risk of complications were analyzed regarding localization, induction, and tachycardia rate.

Table 1. Patient characteristics and concomitant arrhythmias in focal atrial tachycardia

Variable	Women	Men	*P* value
Age (years)	52.8±16.8	52.8±17.9	0.979
Cardiovascular comorbidities			
Hypertension	29 (10%)	33 (17%)	0.026
Ischemic heart disease	6 (2%)	20 (11%)	0.001
Heart failure	6 (2%)	19 (10%)	0.001
Valvular diseases	3 (1%)	1 (0.5%)	0.611
Total	44 (15%)	73 (39%)	0.001
Concomitant arrhythmias			
AVNRT	25 (8%)	13 (7%)	0.564
Atrial fibrillation	13 (4%)	13 (7%)	0.244
Atrial flutter	12 (4%)	13 (7%)	0.182
Accessory pathway	2 (1%)	5 (3%)	0.079
Nonfocal atrial tachycardia	3 (1%)	3 (2%)	0.561
Total	55 (18%)	47 (25%)	0.163

AVNRT - atrioventricular nodal reentrant tachycardia

Statistical analysis

The distribution of each continuous variable was tested for normality using the Kolmogorov-Smirnov test. Normally distributed variables were performed using the Student's t test and are expressed as mean±standard deviation. The categorical variables are expressed in frequencies and percentages. The chi-square tests were used to compare categorical variables. P<0.05 was considered statistically significant. The SPSS version 22.0 software (SPSS Inc., Chicago, IL, USA) was used for all analyses.

Results

Overall, 451 foci were successfully ablated in 436 patients (90%). Complete success, partial success, and failure numbers of acute radiofrequency ablation was 270, 6, and 22 in women and 166, 5, and 18 in men, respectively. No statistically significant difference were found in terms of acute ablation success rate between women and men (p=0.707). In 51 patients, ablation was aborted or failed, the main reasons for which were frequent induction of AF during mapping, high risk of AV-nodal injury, multiple foci, localized focus but repetitive recurrences, and failure of adequate mapping (Table 2). Procedure and fluoroscopy times were 162±65 and 22±18 minutes, respectively, with no significant differences between women and men.

Notably, 80% of the foci were in the right atrium and 20% in the left atrium, with no significant differences between sexes. The most common locations were CT (37%), posteroseptal (14%) and anteroseptal regions (9%), TA (7%) in the right atrium, and the PVs (10%) in the left atrium (Table 3).

Foci located along the CT were more common in women than in men (42% vs. 29%; p=0.023), whereas the opposite was found in the foci located along the TA (5% vs. 11%; p=0.032) and the right atrial appendage (RAA) (1% vs. 3%; p=0.032). Other locations were similarly distributed between men and women (Fig. 1).

More men than women presented with persistent AT (22% vs. 5%; p<0.001). AT occurred spontaneously during the ablation procedure in 28% of men and in 25% of women. Programmed extrastimulation (PES) was more often successfully used for the induction of FAT in women than men (Table 4). Although 46% of women and 38% of men required an isoproterenol to induce tachycardia, only 23% of women and 22% of men needed atropine to start FAT. There was no statistically significant difference between sexes in this regard.

In 82 patients (17%), 102 concomitant arrhythmias were induced, most commonly AV-nodal reentrant tachycardia, AF, and AFL (Table 1). There was no sex difference according to the presence of concomitant arrhythmias.

The average and regional tachycardia cycle lengths in females and males were not statistically different (375±82 vs. 384±106; p=0.371). In other words, there was no sex difference regarding the cycle length of FAT from the same location (Table 4).

Table 2. Preferred mapping techniques and reasons to failed and partially successful ablations

Preferred mapping techniques	Women	Men	*P* value
Conventional catheter mapping	190 (64%)	134 (70%)	0.126
Electroanatomic contact mapping	91 (30%)	46 (24%)	0.167
Noncontact mapping	45 (15%)	18 (10%)	0.099
Causes of failed ablation			
Failure to adequately map foci	9 (3%)	9 (5%)	0.455
High risk of atrioventricular nodal injury	7 (2%)	4 (2%)	0.866
Frequent induction of atrial fibrillation during mapping	3 (1%)	4 (2%)	0.540
Risk of sinus node or phrenic nerve injury		2 (0.7%)	0.688
Left atrial membrane		1 (0.5%)	0.818
Aborted owing to complication	1 (0.3%)		0.425
Reasons for partial succeed relations			
Multiple foci	4 (1.3%)	5 (2.6%)	0.486
Localized focus but repetitive recurrences	2 (0.7%)		0.688

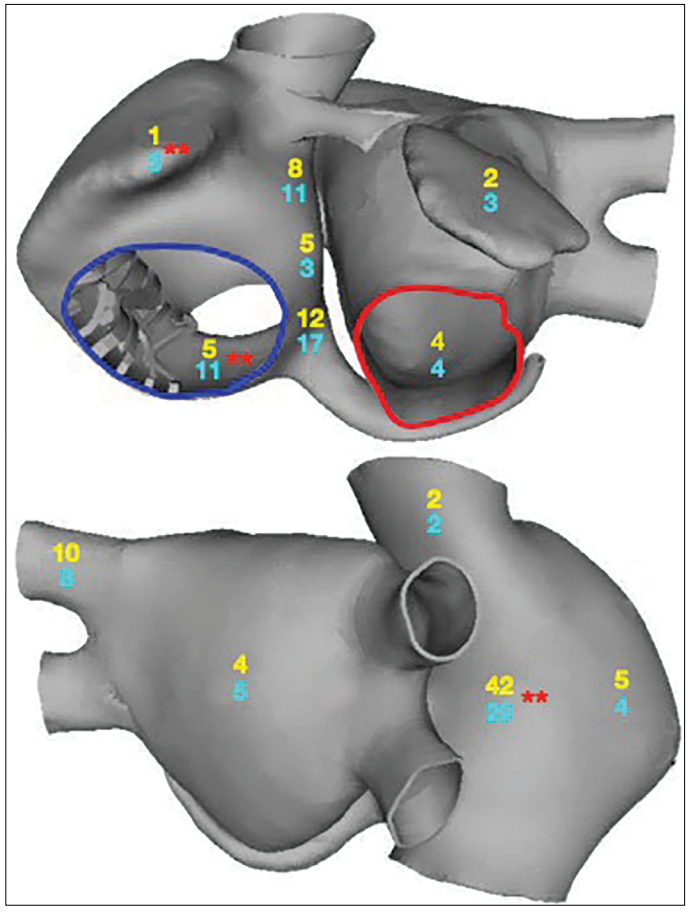

Figure 1. The localization ratios of ectopic atrial tachycardia shown as percentage in women and men. The upper and lower figures symbolize the anteroposterior and posteroanterior views of the atriums, respectively. The yellow colors represent the ratio in women, whereas blue color shows the ratio in men. The total ratio of ectopic atrial tachycardia from all 4 pulmonary veins (PVs) has indicated on the left superior pulmonary vein
**Significantly different location ratios of focal atrial tachycardia in men and women

Discussion

To the best of our knowledge, this is the largest study comparing the localization and characteristics of FAT between men and women. The main finding is a different distribution of focal between women and men that women have a higher proportion of AT from the CT (42% vs. 29%) and men have a higher proportion of AT from the TA and RAA. The number of persistent AT was greater in men than in women. The distribution of FAT for the whole group was similar to the previous studies, in which CT was the most common origin of FAT in both women and men (3, 5, 7).

A higher proportion of CT localization in women as the origin of FAT could be explained by the differences in the structure's anatomy between men and women. Sánchez-Quintana et al. (8) studied on 97 human necropsy hearts and found that the length and width of the CT are greater in women than in men, particularly in the lower part of the CT. Considering the smaller right atrium and body surface area in women than in men, CT constitutes a larger part of the right atrium in women. Although the TA and RAA were uncommon sources of FAT, they were more frequent origins in men than in women. Similarly, although Morton et al. (9) found the TA as a 2 times more common origin of FAT in men, Roberts-Thomson et al. (10) have discovered the RAA as a 9-fold frequent source of FAT in men than in women. Likewise, Freixa et al. (11) released very important article on the tachycardias from the RAA. They also mapped the FAT by conventional or three-dimensional mapping system and showed the significant predominance of male sex in terms of RAA localization (11). Finally, a study on AT-induced cardiomyopathy was conducted by Medi et al. (12), which revealed that RAA-originated ATs are 7 times more common in men than in women. All these data clearly support our findings and indicate that although CT is highly common in women, TA and RAA-originated FATs is more common in men than in women.

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Table 3. Localization of focal atrial tachycardia foci in both women and men

Region	Total	Women	Men	*P* value
Right atrial total	368 (80%)	225 (80%)	143 (80%)	0.988
Anteroseptal	43 (9%)	24 (8%)	19 (11%)	0.475
Midseptal	19 (4%)	14 (5%)	5 (3%)	0.263
Posteroseptal and coronary sinus os	64 (14%)	33 (12%)	31 (17%)	0.111
Crista terminalis	171 (37%)	119 (42%)	52 (29%)	0.023
Tricuspid annulus	33 (7%)	14 (5%)	19 (11%)	0.032
Right atrial appendage	8 (2%)	2 (1%)	6 (3%)	0.032
Right atrium other	22 (5%)	14 (5%)	8 (4%)	0.807
Superior vena cava	8 (2%)	5 (2%)	3 (2%)	0.941
Left atrial total	94 (20%)	58 (20%)	36 (20%)	0.922
Pulmonary veins	45 (10%)	30 (10%)	15 (8%)	0.452
Mitral annulus	17 (4%)	10 (4%)	7 (4%)	0.844
Left atrial appendage	10 (2%)	5 (2%)	5 (3%)	0.467
Left atrium other	22 (4%)	13 (4%)	9 (5%)	0.839
Both atrial total	**462**	**283**	**179**	

Table 4. Characteristics of focal atrial tachycardias in both sexes

Locations	Women TCL	Men TCL	*P* value
Pulmonary veins	311±52	269±72	0.081
Crista terminalis	378±72	375±93	0.878
Anteroseptal	383±82	393±103	0.729
Midseptal	388±77	401±101	0.734
Coronary sinus ostium	395±78	385±87	0.673
Right atrium	395±101	410±104	0.778
Left atrium	359±112	359±76	0.994
Tricuspid annulus	405±68	412±94	0.852
Superior vena cava	420±81	407±91	0.919
Right atrial appendage	375±106	395±68	0.745
Left atrial appendage	468±137	430±121	0.732
Average TCL	375±82	384±106	0.371
Tachycardia induction			
PES only	122 (41%)	49 (26%)	0.007
PES+isoproterenol	68 (23%)	34 (18%)	0.222
PES+atropine	18 (6%)	11 (6%)	0.913
Spontaneous	75 (25%)	53 (28%)	0.593
Persistent	15 (5%)	42 (22%)	<0.001

TCL - tachycardia cycle length in milliseconds; PES - programmed extrastimulation

More men than women presented with persistent AT (22% vs. 9%). An inflammation is a well-known underlying precursor of persistent atrial arrhythmias such as AF and AT. Chung et al. (13) have compared the level of C-reactive protein (CRP) between patients with atrial arrhythmias and healthy members of the control group. They have detected significantly higher levels of CRP in patients with ATs and fibrillation than the members of the control group. Furthermore, coronary artery disease and heart failure undoubtedly facilitate the formation of ischemia, inflammation, or atrial remodeling in the atriums (14), which were significantly higher in our male patients. Alternatively, Bukowska et al. (15) revealed the favorable effect of estrogen on inflammation in atrial tissue. Only 13% of our female patients were more than 60 years old, and it points to the higher levels of estrogen in women than in men. All these data may explain the higher ratio of persistent AT in men in our study. Hu et al. (4) published one of the largest trials about focal AT that involved 298 patients, and they also reported a higher incidence of persistence FAT in men than women.

PES was more often successfully used for the induction of FAT in women than in men (70% vs. 50%). This finding was not the main aim of the study and was noticed as a result of statistical comparison. Morris GM et al. have also found the focal AT as more likely to be inducible with PES in women (7). FAT frequently arises as a result of abnormal automaticity and is difficult to induce during an electrophysiological study and needs some intravenous medication to induce, which we had to use either isoproterenol or atropine. Alternatively, PES facilitates both triggered activity and reentry mechanism and thus initiation of FAT. Even if it is difficult to give a clear information about the underlying mechanism of FAT because of the mixed use of PES and isoproterenol infusion in the initiation of tachycardia, it seems that different reasons play a role in the pathophysiology of FAT in different sexes.

The ratio of FATs from the right and left atrium was exactly the same in both sexes. Although 80% of all FATs originate from RA, others are seen in the left atrium. This situation can be explained by the fact that RA has the more complex structure and different innervation pattern than LA. Another study by Xia et al. (16) has also showed that RA accounts for 80% as an origin of

FAT but although they encountered more right-sided tachycardia in women, left ATs were seen more in men.

Although some tachycardias from different parts of the atrium have had various cycle lengths, the average and regional tachycardia cycle lengths in female and males were not statistically different. In other words, there was no sex difference regarding the cycle length of FAT from the same location. The reasons for the statistically insignificant different cycle lengths of FAT from various regions of the atria are not fully known but underlying anatomic and physiologic properties and degree of anisotropy in PVs, CT, and pure atrial myocardium differ significantly and are considered of importance.

Study limitations

Differences in the basic characteristics of patients, such as ischemic heart disease and heart failure, may affect the results, particularly the underlying mechanism of tachycardia. In addition, restricted data about the levels of estrogen in both pre- and postmenopausal women made it difficult to explain the primary reason of FAT.

Conclusion

The distribution of FAT in women and men is different. In addition, persistent FAT seems more often in men than in women. The different distribution, persistency, and induction pattern of FAT should be considered in the successful management of this tachycardia.

Conflict of interest: None declared.

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