Frequency and predictors of tachycardia-induced cardiomyopathy in patients with persistent atrial flutter

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BACKGROUND: There are few data on the frequency and predictors of tachycardia-induced cardiomyopathy (TICM) in patients with persistent atrial flutter.

OBJECTIVES: To examine the incidence of TICM in patients undergoing ablation for persistent atrial flutter, and to examine predictors for the development of TICM.

METHODS AND RESULTS: One hundred eleven patients met the inclusion criteria for the present study. Twenty-eight of 111 (25%) patients had cardiomyopathy before ablation. Sixteen of 28 (57%) patients showed significant improvement in their left ventricular (LV) function postablation. LV function improved to normal in 12 of 16 (75%) patients. Nineteen of 28 (68%) cardiomyopathy patients had preablation LV function in the range in which they would be considered for an implantable cardioverter defibrillator for primary prevention of sudden cardiac death. In nine of 19 (47%) patients, the ejection fraction improved such that an implantable cardioverter defibrillator was no longer indicated. In multivariate analysis, average ventricular rate during atrial flutter was the only independent predictor of reversibility of cardiomyopathy ($P=0.013$).

CONCLUSIONS: Sixteen of 28 (57%) cardiomyopathy patients with persistent atrial flutter had significantly improved LV function postablation. In 75% of these patients, LV function improved to normal.

Key Words: Atrial flutter; Cardiomyopathy; Implantable cardioverter defibrillator; Predictors; Tachycardiomyopathy

Tachycardia-induced cardiomyopathy (TICM) is important to recognize because the left ventricular (LV) dysfunction is partially or wholly reversible (1). The first practice guidelines for diagnosing and managing TICM were recently published (2). Previously, it was considered to be a rare cause of cardiomyopathy (1,3,4). Furthermore, some patients have TICM superimposed on underlying cardiomyopathy (1,5,6). Few data related to predictors of reversibility of LV dysfunction in these patients have been published. This latter point is particularly relevant in the current era of primary prevention implantable cardioverter defibrillator (ICD) implantation. Potentially, there is a group of patients who may not require ICD implantation if LV function improves after reversal of the arrhythmia.

The objectives of the present study were to examine the incidence of TICM in patients undergoing ablation for persistent typical atrial flutter, examine predictors for the development of TICM and analyze predictors of the reversibility of cardiomyopathy in patients with persistent atrial flutter and LV dysfunction.

Fréquence et prédicteurs de la cardiomyopathie induite par la tachycardie chez des patients présentant un flutter auriculaire persistant

HISTORIQUE : On dispose de peu de données sur la fréquence et les prédicteurs de la cardiomyopathie induite par la tachycardie (MCIT) chez des patients souffrant de flutter auriculaire persistant.

OBJECTIF : Analyser l'incidence de la MCIT chez des patients devant subir un traitement par ablation pour flutter auriculaire typique persistant et les prédicteurs de la MCIT.

MÉTHODES ET RÉSULTATS : Cent onze patients répondaient aux critères d'inclusion de la présente étude. Vingt-huit patients sur 111 (25 %) souffraient de cardiomyopathie avant le traitement par ablation. Seize patients sur 28 (57 %) ont manifesté une amélioration significative de leur fonction ventriculaire gauche (VG) après le traitement par ablation. La fonction VG a été ramenée à la normale chez 12 patients sur 16 (75 %). Dix-neuf patients souffrant de cardiomyopathie sur 28 (68 %) présentaient une fonction VG pré-ablative qui les classait parmi les candidats au défibrillateur implantable en prévention primaire. Chez neuf patients sur 19 (47 %), la fraction d'éjection s'est améliorée au point où le défibrillateur implantable n'était plus jugé nécessaire. À l'analyse multivariée, la fréquence ventriculaire moyenne durant le flutter auriculaire a été le seul prédicteur indépendant de la réversibilité de la cardiomyopathie ($p = 0,013$).

CONCLUSIONS : Seize patients atteints de cardiomyopathie sur 28 (57 %) souffrant de flutter auriculaire persistant présentaient une fonction VG significativement meilleure après le traitement par ablation. Chez 75 % de ces patients, la fonction VG est revenue à la normale.

METHODS

Inclusion criteria

All consecutive patients who underwent successful radiofrequency catheter ablation for persistent typical atrial flutter from 1998 to 2006 at the University of Ottawa Heart Institute (Ottawa, Ontario) were assessed. Ablation was performed using the standard protocol. Success was defined as termination of atrial flutter (if ablation was performed during atrial flutter) and achievement of bidirectional cavotricuspid isthmus conduction block in all patients. If patients had recurrent atrial flutter during the follow-up examination, repeat ablation was performed. All patients who underwent an LV function assessment before their ablation procedure were included in the study.

LV function quantification

LV function was quantified as grade 1 (normal; ejection fraction [EF] 50% or greater), grade 2 (mild dysfunction; EF 40% to 49%), grade 3 (moderate dysfunction; EF 30% to 39%), grade 4 (severe dysfunction; EF 20% to 29%) or grade 5 (very severe dysfunction; EF 20% or less).

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Figure 1) Flow diagram illustrating recruitment of the cohort. AFI Atrial flutter; CM Cardiomyopathy; LV Left ventricular; TICM Tachycardia-induced cardiomyopathy; VR Ventricular response

Definition of TICM

A patient was considered to have TICM if there was an improvement of LV function of at least one grade between pre- and postablation.

Ventricular response during atrial flutter

Ventricular response during atrial flutter was assessed using a Holter monitor (a computer read the average heart rates during the monitoring period), and the patient was stated to be in atrial flutter throughout the study. If a Holter monitor was not available, the ventricular response seen on electrocardiograms during persistent atrial flutter was used. Ventricular response seen on all electrocardiograms during atrial flutter was assessed and the mean response was calculated.

Other variables

Any history of atrial fibrillation, hypertension, significant structural or valvular disease, coronary artery disease, myocardial infarction and beta-blocker use was recorded. The variables of coronary artery disease, previous myocardial infarction and significant structural or valvular heart disease were combined into a single variable called heart disease for statistical analysis. Rhythm data were also collected during LV function quantification.

Statistics

All variables were considered to be nonparametric. Quantitative variables were analyzed using Wilcoxon's two-sample test. Categorical variables were analyzed using Fisher's exact test. Quantitative variables are presented as mean $\pm$ SD or median (interquartile range) where appropriate. All variables with $P < 0.20$, except 'days to ablation from LV function test', were entered into a stepwise multiple logistic regression model. The statistics were calculated using SAS version 9.1 (SAS Institute Inc, USA).

Ethics

The present study complies with the Declaration of Helsinki. The study protocol was reviewed and approved by the ethics board of the University of Ottawa Heart Institute.

RESULTS

Patient characteristics

A total of 111 patients met the inclusion criteria for the present study. Figure 1 is a flow diagram illustrating cohort recruitment. Five patients required two sessions of ablation.

Figure 2) Ventricular response in 28 patients with cardiomyopathy stratified by the presence (left; $n=16$) or absence (right; $n=12$) of tachycardia-induced cardiomyopathy

Preablation LV function

Preablation LV assessments were performed by echocardiography in 94 patients (85%) and radionuclide ventriculography in 17 (15%). LV dysfunction was detected in 28 of 111 (25%) patients (nine had grade 2 dysfunction, 10 had grade 3, seven had grade 4 and two had grade 5).

Frequency of TICM

LV function assessments were performed 103 days (range 64 to 360 days) postablation. Some degree of TICM was evident in 16 of 28 (57.1%) cardiomyopathy patients. Ventricular function improved to normal in 12 of 16 (75%) patients (Figure 2). The overall frequency of TICM in patients with persistent atrial flutter was 16 of 111 (14.4%). Before ablation, 19 of 28 (68%) patients had LV dysfunction within the range (ie, less than 30% to 40%) in which guidelines (7) suggest patients should be considered for primary prevention ICD placement. Subsequently, nine of 19 (47%) patients improved so that their LV dysfunction was no longer within this range.

Variables associated with the development of TICM

For this analysis, TICM patients were compared with patients with other cardiomyopathy or normal LV function grouped together. The univariate analysis is shown in Table 1. In multiple logistic regression analysis, the only independent predictor was 'not sinus rhythm' at the time of the preablation LV function test (OR 6.48 [95% CI 1.31 to 32.07]; $P=0.010$).

Predictors of reversibility of cardiomyopathy

Table 2 details the univariate comparison of patients with irreversible cardiomyopathy ($n=12$) and patients who had TICM ($n=16$). Univariate predictors were history of myocardial infarction ($P=0.019$) and ventricular response during atrial flutter ($P=0.009$). In multiple regression analysis, the only independent predictor of TICM was ventricular response ($P=0.013$). History of infarction was not an independent predictor ($P=0.102$). The mean ventricular response in patients with TICM was 109 ± 17.8 beats/min and was 84 ± 23.1 beats/min in patients with nonreversible cardiomyopathy (Figure 3). Seventy-five per cent of patients with a ventricular response of 100 beats/min or greater improved compared with only 25% of patients with a ventricular response of less than 100 beats/min ($P=0.0531$). All four patients with a ventricular response of greater than 120 beats/min showed improvements in their LV function postablation.

DISCUSSION

TICM is an important cause of reversible cardiomyopathy. In the present study, 57% of patients with persistent atrial flutter demonstrated some degree of TICM. In 75% of the patients, LV function improved to normal (Figure 2). The overall frequency of TICM in patients with persistent atrial flutter was 14.4%. The only independent predictor of

TABLE 1
Comparison of tachycardia-induced cardiomyopathy (TICM) patients with all other patients

Variables	TICM (n=16)	Normal LV function + nonreversible CM (n=95)	P
Age, years, median (range)	62 (51–68)	58 (52–66)	0.59
Men	14 (88)	75 (79)	0.73
Previous atrial fibrillation	11 (69)	73 (77)	0.53
Previous myocardial infarction	3 (19)	13 (14)	0.70
Heart disease	12 (75)	47 (49)	0.10
Beta-blocker	6 (38)	40 (42)	0.79
Sinus rhythm during LV function test before ablation*	2/12 (17)	35/62 (56)	0.02
Average VR in atrial flutter, median (range)	112 (102–122)	100 (78–128)	0.32

Data presented as n (%) unless otherwise specified. *Data available in 74 patients. CM Cardiomyopathy; LV Left ventricle; VR Ventricular response

reversible LV dysfunction in patients with cardiomyopathy and persistent atrial flutter was ventricular response.

Our results add to the accumulating evidence that TICM is more common than previously considered. Luchsinger and Steinberg (6) found that six of 11 (55%) patients with persistent atrial flutter had some degree of reversible cardiomyopathy. Considerably more data exist on patients with atrial fibrillation. Recently, Gentlesk et al (8) studied 50 patients with decreased EF undergoing therapeutic ablation for paroxysmal or persistent atrial fibrillation. Of those 50 patients, EF improved in 47 (94%) and normalized in 36 (72%) patients. Hsu et al (5) found that 42 of 58 (72%) patients with atrial fibrillation and congestive heart failure had marked improvement (defined as greater than 20% and/or normal) in ventricular function after atrial fibrillation ablation. Atrial fibrillation-induced TICM has also been shown to improve with good rate control (9), cardioversion (9–11) or after atrial ventricular node ablation and pacemaker implantation (12,13).

In our study, the only independent predictor of developing TICM was 'not sinus rhythm' at the time of the preablation LV function test (OR 6.48 [95% CI 1.31 to 32.07]). This finding may reflect a greater duration of atrial flutter in patients who developed TICM. Alternatively, it may be due to the limitations of LV function assessment during atrial arrhythmia (14). However, these limitations are likely to be reduced in patients with atrial flutter rather than atrial fibrillation, due to lesser RR interval irregularity.

We also examined the related but importantly different question of what predicts reversibility of LV dysfunction in patients with cardiomyopathy and persistent atrial flutter. We found that the only independent predictor was ventricular response during arrhythmia. The mean ventricular response in patients with TICM was 109 ± 17.8 beats/min and the mean ventricular response in patients with nonreversible cardiomyopathy was 84 ± 23.1 beats/min (Figure 3). Seventy-five per cent of patients with a ventricular response of 100 beats/min or greater improved compared with only 25% of patients with a ventricular response of less than 100 beats/min. Additionally, all four patients with a ventricular response of greater than 120 beats/min showed improvements in their EF. However, it should be noted that two patients with a well-controlled ventricular response (ventricular response of less than 80 beats/min) had evidence of TICM. These findings indicate that ventricular response is likely the most important factor in the etiology of TICM, but additional factors may be relevant in some patients. These data are consistent with other evidence. For example, Hsu et al (5) documented that some patients with apparent reasonable rate control during atrial fibrillation had improved LV function following successful atrial fibrillation ablation. Similarly, Gentlesk et al (8) found that

TABLE 2
Comparison of tachycardia-induced cardiomyopathy (TICM) patients with nonreversible cardiomyopathy (CM)

Variables	TICM (n=16)	Non reversible CM (n=12)	P
Age, years	62 (51–68)	65 (61–74)	0.26
Men, n (%)	14 (88)	12 (100)	0.49
Previous atrial fibrillation, n (%)	11 (69)	8 (67)	1.00
Previous myocardial infarction, n (%)	3 (19)	8 (67)	0.02
Heart disease, n (%)	12 (75)	11 (92)	0.36
Beta-blocker, n (%)	10 (63)	9 (75)	0.69
Sinus rhythm during LV function test before ablation*, n (%)	2/12 (17)	3/12 (25)	0.35
Days to ablation from LV function test	61 (14–152)	91 (70–166)	0.19
Days since ablation to LV function test	89 (55–149)	142 (76–431)	0.28
Average VR in atrial flutter	112 (102–122)	83 (70–108)	0.01

Data presented as median (range) unless otherwise specified. *Data available in 24 patients. LV Left ventricle; VR Ventricular response

Figure 3 Left ventricular (LV) function grade pre- and postablation in 28 patients with cardiomyopathy. The broken lines indicate single patient data. The solid lines indicate multiple patient data, with the thickness of the line relative to the number of patients (ie, 6 patients improved from grade 3 to grade 1; 4 patients improved from grade 2 to grade 1; 4 patients were unchanged at grade 2; 3 patients were unchanged at grade 3; 2 patients were unchanged at grade 4; and 2 patients improved from grade 4 to grade 1)

only 22% of TICM patients had shown tachycardia at greater than 100 beats/min on preablation electrocardiography. It has been suggested that loss of atrial transport (15) and rhythm irregularity (8,16) may play a role in some TICM patients.

The potential for any reversibility of LV dysfunction should always be explored to improve patient symptoms and mortality. The first practice guidelines for diagnosing and managing TICM were published recently (2). In addition, EF is the key factor in deciding whether to implant a prophylactic ICD in these patients (7). ICD therapy for primary prevention is now recommended for patients who have an LV range of 30% or lower to 40%. In our study, 19 patients had an initial EF of 40% or lower and nine of 19 (47%) improved to greater than 40% after successful ablation of their atrial flutter. Using current guidelines, an ICD would no longer be considered in these patients. However, it should also be noted that an ablation and reassessment strategy has some risks. One contemporaneous patient, who would have been included in the study, had a sudden cardiac death four weeks following successful atrial flutter ablation. His preablation EF was 24% and he was awaiting his repeat EF to assess the need for a primary prevention defibrillator. Hence, an ablation and reassessment strategy should be cautiously considered and possibly reserved for patients with poor rate control during atrial flutter and/or those with a borderline initial EF. In addition, perhaps some of these patients should be provided with an automated external defibrillator while awaiting reassessment of their EF.

Limitations

The present study has a number of limitations, largely reflecting the observational nature of the study. There was no standard preablation LV function test time or standard follow-up time. LV function is reported by change in LV grade as opposed to LV size and EF. Also, many patients had ventricular response assessed from all available electrocardiograms, which is likely less accurate than a 24 h average obtained by Holter monitoring. Third, we cannot exclude an element of selection bias in the cohort. Finally, we did not collect information on concurrent medical therapy used for patients with heart failure such as angiotensin-converting enzyme inhibitors or medications used for rate control such as amiodarone, calcium channel blockers or digoxin.

CONCLUSION

We determined that TICM is not rare in patients with persistent atrial flutter and cardiomyopathy. We found that 57% of our cohort had some degree of reversibility of LV dysfunction and in 75% of these patients, EF improved to normal. The only independent predictor of reversible dysfunction in patients with cardiomyopathy and persistent atrial flutter was ventricular response during atrial flutter. Furthermore, in our study, 19 patients were initially candidates for primary prevention ICD, but after ablation, nine of 19 (47%) patients improved such that they would no longer be considered for ICD placement.

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