Clinical Characteristics, Treatment, and Outcome of Tachycardia Induced Cardiomyopathy

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SUMMARY

Tachycardia-induced cardiomyopathy is characterized by ventricular systolic dysfunction and congestive heart failure resulting from persistent or highly frequent tachyarrhythmias with uncontrolled heart rate. While reversible and often considered benign, few studies have examined the outcome of the disorder.

The clinical characteristics, treatment, and long-term outcomes of 12 consecutive patients with tachycardia-induced cardiomyopathy (9 men, age, 51.9 ± 17.6 years) were studied. The mean period between the occurrence of tachyarrhythmias and the development of congestive heart failure was 26.0 ± 34.3 days. The mean heart rate on admission was 156.3 ± 28.7 beats/min. All patients had severe heart failure with a NYHA functional class of 2.3 ± 0.5 , left ventricular ejection fraction of 0.32 ± 0.10 , and brain natriuretic peptide level of 505.7 ± 449.1 pg/mL. In all patients, cardiac dysfunction recovered after 53.5 ± 61.3 days. During the follow-up of 53 ± 24 months, 2 patients had a recurrence of heart failure with uncontrolled tachyarrhythmia and 1 patient died suddenly.

In tachycardia-induced cardiomyopathy, recurrent heart failure with uncontrollable tachyarrhythmia and sudden death were observed after recovery from cardiac dysfunction. A substrate for heart failure and/or life-threatening arrhythmia might persist, and careful, long-term follow-up seems required. (Int Heart J 2008; 49: 39-47)

Key words: Arrhythmia, Cardiomyopathy, Sudden death, Heart failure

TACHYCARDIA-INDUCED cardiomyopathy is characterized by ventricular systolic dysfunction and congestive heart failure that are caused by persistent or highly frequent tachyarrhythmias with rapid heart rate.¹⁻³⁾ Tachyarrhythmias that can cause tachycardia-induced cardiomyopathy include atrial fibrillation, atrial flutter, atrial tachycardia, accessory pathway tachycardia, atrioventricular nodal reentry tachycardia, incessant ventricular tachycardia, and repetitive ventricular

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premature beats.⁴⁻⁷⁾ While tachycardia-induced cardiomyopathy usually presents with significant cardiac enlargement, reduced ventricular wall thickness, and impaired ventricular contraction similar to dilated cardiomyopathy, the cardiac abnormalities normalize with control of the tachyarrhythmia and heart failure.⁸⁻¹⁰⁾

Although tachycardia-induced cardiomyopathy is believed to be benign, few reports have described the outcome of this condition since it was first recognized in 1913.^{8,11,12)} However, sudden death and heart failure recurrence after normalization of cardiac function was recently reported in tachycardia-induced cardiomyopathy suggesting that careful follow-up is required.¹²⁾ In this study, we investigated the clinical characteristics and long-term outcome in patients with tachycardia-induced cardiomyopathy.

METHODS

Patients: This study included 12 consecutive patients (9 men, 3 women; mean age, 51.9 ± 17.6 years; range, 12 to 72 years) who were admitted to our hospital from January 1999 to December 2004 with congestive heart failure due to tachycardia-induced cardiomyopathy (Table). A patient was included if they developed heart failure after the onset of tachyarrhythmia and demonstrated reversal of cardiac dysfunction after controlling the tachycardia. All patients underwent an echocardiogram on admission and after improvement of congestive heart failure and cardiac catheterization including left ventriculography and a coronary angiogram. Patients with heart failure caused by a condition other than tachyarrhythmia, such as ischemic heart disease, valvular heart disease, and drug- or alcohol-induced cardiomyopathy, were excluded.

Treatment: Selection of antiarrhythmic therapy was based on the individual tachyarrhythmia. If indicated, catheter ablation was considered to control heart rhythm. However, catheter ablation was not available for atrial fibrillation at the time of entry into this study. Cardioversion was attempted to restore sinus rhythm in patients with atrial fibrillation. Rate control therapy was optimized with Holter recording. Beta-blockers were administered in all patients who required rate control and the dose was increased if tolerated. Verapamil and/or digoxin were combined with beta-blockers when required.

Follow-up: After achieving control of the tachycardia and heart failure, patients were discharged and followed-up at an outpatient clinic every one to two month(s). Patients whose tachyarrhythmias were successfully ablated visited the clinic once a year or more frequently.

Data analysis: We assessed the clinical characteristics, treatment efficacy, and the long-term outcomes of patients with tachycardia-induced cardiomyopathy. All numerical data are presented as the mean $\pm$ SD. Paired values were compared

Table. Characteristics of the Tachycardia-Induced Cardiomyopathy

Patient	Age (years)	Sex	Arrhythmia	Time* (days)	Presentation				The -rapy	After treatment			Time† (days)	Recu -rrent	Sudden death
					HR (bpm)	NYHA	BNP	EF		HR (bpm)	NYHA	EF			
1	40	F	AF	20	175	2	103	0.25	Rate	78	1	0.53	14	N	N
2	59	F	AF	30	130	3	760	0.28	Rate	60	1	0.54	34	Y	N
3	67	M	AF, WPW	6	170	2	N/A	0.27	Both	86	1	0.56	64	N	N
4	59	M	AFL	20	170	2	322	0.35	Rate	60	1	0.51	56	N	N
5	52	M	AFL	7	150	2	73	0.29	Rate	80	1	0.65	62	Y	N
6	49	F	AFL	30	160	3	305	0.51	Rate	70	1	0.67	35	N	N
7	72	M	AFL	14	160	3	1330	0.25	Rate	76	1	0.52	240	N	Y
8	63	M	AFL	12	150	3	N/A	0.47	RF	74	1	0.65	21	N	N
9	50	M	AFL, WPW	14	100	2	14	0.31	RF	70	1	0.58	21	N	N
10	30	M	AVNRT	28	190	2	788	0.25	RF	70	1	0.50	21	N	N
11	12	F	IVT	120	160	2	857	0.17	RF	60	1	0.54	50	N	N
12	70	M	IVT	- ‡	200	2	N/A	0.43	RF	66	1	0.51	24	N	N
Mean	51.9 ± 17.6			26.0 ± 34.3	156.3 ± 28.7	2.3 ± 0.5	505.7 ± 449.1	31.9 ± 10.2		70.8 ± 8.4	1.0 ± 1.0	54.3 ± 10.4	53.5 ± 61.3		

* Time from the occurrence of symptoms due to tachyarrhythmia to hospitalization due to congestive heart failure. † Time from hospitalization to normalization of left ventricular dysfunction. ‡ a patient did not have any prior symptoms suggesting tachyarrhythmia. Arrhythmia indicates arrhythmia believed to be the cause of tachycardia-induced cardiomyopathy; HR, heart rate; NYHA, New York Heart Association functional class; BNP, brain natriuretic peptide; EF, ejection fraction; AF, atrial fibrillation; WPW, Wolff-Parkinson-White syndrome; AFL, atrial flutter; AVNRT, atrioventricular nodal reentrant tachycardia; IVT, idiopathic ventricular tachycardia from the right ventricular outflow tract; and RF, radiofrequency catheter ablation.

using the paired Student's *t*-test. Time-to-event curves describing the proportion of patients who remained event-free were constructed using the Kaplan-Meier method. All statistical analyses were performed with SPSS, version 12.0 (SPSS Inc, Chicago, IL). Differences were considered significant at $P < 0.05$.

RESULTS

Patient characteristics: The Table presents the clinical characteristics of patients enrolled in this study. The mean period from the occurrence of symptoms due to tachyarrhythmias to the hospitalization due to congestive heart failure was 26.0 ± 34.3 days (range, 3 to 120 days). Mean heart rate on admission was 156.3 ± 28.7 beats/min (range, 100 to 200 beats/min). All patients had severe cardiac dysfunction with a mean New York Heart Association functional class of 2.3 ± 0.5 (range, 2 to 3) and a mean left ventricular ejection fraction of 0.32 ± 0.10 (range, 0.17 to 0.51) as assessed by echocardiography. Mean wall thickness was 9.6 ± 2.2 mm and 9.4 ± 2.0 mm for the septum and posterior wall of the left ventricle, respectively, and no patient had left ventricular hypertrophy. Mean brain natriuretic peptide level on admission to the hospital was 505.7 ± 449.1 pg/mL (range, 14 to 1330 pg/mL).

Causative tachycardias: The most likely cause of the heart failure was atrial fibrillation in 3 patients, atrial flutter in 6, atrioventricular nodal reentrant tachycardia in 1, and idiopathic ventricular tachycardia originating from the right ventricular outflow tract in 2. One patient with atrial fibrillation and one with atrial flutter also had an antegrade accessory atrioventricular pathway. One patient with

atrial fibrillation (patient 2) had hyperthyroidism treated by methimazole.

Treatment of tachycardias: Catheter ablation was performed for the causative arrhythmia and was successful in 6 patients (50%), including 3 patients with atrial flutter, 1 with atrioventricular nodal reentrant tachycardia, and 2 with idiopathic ventricular tachycardia. Two of 3 patients with atrial fibrillation received only medication to control their heart rate, while the remaining patient received both medication for rate control and catheter ablation to eliminate an accessory pathway. Beta-blockers were administered to control ventricular rate in 7 patients (58%), including 4 patients with atrial flutter and 3 with atrial fibrillation. No patient received class I or III antiarrhythmic drugs.

Following treatment, the heart rate decreased to 70.8 ± 8.4 beats/min (range, 60 to 86 beats/min, $P < 0.001$ compared to that at admission) and the New York Heart Association functional class improved by one class in all patients (1.0 ± 0.0 , $P < 0.001$). The ejection fraction recovered to 0.54 ± 0.10 (range, 0.50 to 0.67, $P < 0.001$) during a mean of 53.5 ± 61.3 days (range, 14 to 240 days) after admission to the hospital.

Recurrence of tachycardia-induced cardiomyopathy: During the follow-up period of 53 ± 24 months (range, 6-87 months), 2 patients had a recurrence of tachycardia-induced cardiomyopathy and one died suddenly. The event free rate (free from recurrent heart failure and sudden death) at 3 years was 73% as estimated by Kaplan-Meier analysis (Figure 1). All 3 patients with an event received rate control therapy with beta-blockers but not catheter ablation. One patient (patient 5) developed atrial flutter with uncontrolled heart rate during therapy with propranolol (Figure 2). Catheter ablation was refused at the initial episode of tachycar-

Figure 1. Incidence of heart failure recurrence and sudden death. Kaplan-Meier method was used to obtain the event-free curve. Events include recurrence of heart failure and sudden death.

Figure 2. Echocardiography of recurrent tachycardia-induced cardiomyopathy.

A: A 52-year-old man presented with congestive heart failure accompanied by a decreased left ventricular ejection fraction of 0.29 and atrial flutter with a heart rate of 160 beats/min. **B:** After 2 months, the ejection fraction normalized to 0.65 with maintenance of sinus rhythm and conventional treatment for heart failure. **C:** The patient redeveloped heart failure with an ejection fraction of 0.26 three months after recovery from the initial event. **D:** The ejection fraction normalized to 0.57 again with successful catheter ablation and control of heart failure.

dia-induced cardiomyopathy. Another patient with atrial fibrillation (patient 2) was in a hyperthyroid state at recurrence, while thyroid function had been controlled well before the recurrence. The period from the occurrence of symptom onset from tachyarrhythmia to the admission due to recurrence of congestive heart failure was 12 days and 1 day in patients 2 and 5, respectively. The heart rate at presentation of the second episode of heart failure was 130 beats/min (patient 2) and 140 beats/min (patient 5). The ejection fraction declined to a level similar to that of the initial event (0.37 and 0.26 in patients 2 and 5, respectively). Patient 2 received increased dosages of propranolol and methimazole, and patient 5 underwent successful catheter ablation for atrial flutter. After control of tachycardia, the ejection fraction normalized to 0.69 and 0.57 in patients 2 and 5, respectively, and there was no repeated worsening of heart failure for more than 2 years.

Sudden death: During the follow-up, one patient with atrial flutter died suddenly 48 months after the presentation of tachycardia-induced cardiomyopathy (patient 7). This death was unexpected and there were no prior symptoms suggesting tachyarrhythmia or congestive heart failure. At the initial presentation of heart failure, cardiac function was severely depressed with the highest level of brain natriuretic peptide in this study group (Table). No cardiac disease or hypertrophy was identified as a cause of heart failure by echocardiogram or catheterization. Catheter ablation was rejected and carvedilol was administered with enalapril. Cardiac dysfunction persisted, requiring approximately 8 months for recovery of the ejection fraction to 0.52. During follow-up, the heart rate had been well controlled at around 80 beats/min at his visit to the outpatient clinic and he had continued receiving carvedilol and enalapril.

DISCUSSION

In this study, tachycardia-induced cardiomyopathy occurred about 1 month after the development of causal tachyarrhythmia based on the symptoms and cardiac function recovered to a normal level after approximately 2 months. Although the recurrence of heart failure and sudden death occurred after normalization from cardiac dysfunction in 3 of 12 patients (25%), this disorder is considered reversible.

Recurrent cardiac dysfunction: There were 2 patients with recurrent worsening of congestive heart failure, possibly due to uncontrolled tachyarrhythmia, although 1 patient was also in a hyperthyroid state when the cardiac dysfunction reappeared. In tachycardia-induced cardiomyopathy, recurrent cardiac dysfunction was still reversible to the prior normal level. However, an uncontrolled heart rate led to heart failure more rapidly at the second episode compared to the first one, suggesting that latent myocardial disorder is persistent after normalization of cardiac dysfunction. Some findings in human and animal studies support the hypothesis. In experimental models, cardiomyopathy induced by rapid pacing is associated with several changes in myocardial structure and function, and apoptosis.^{6,13,14)} Some of these changes persist after the discontinuation of pacing. Myocardial glucose metabolism is impaired in patients with tachycardia-induced cardiomyopathy and the abnormality continues for at least 6 months despite improvement in cardiac function.¹⁵⁾ Sustained myocardial abnormalities may provide a substrate for recurrence of heart failure.

Interestingly, the patients who experienced sudden death or recurrent heart failure seemed to have severe systolic dysfunction; the mean left ventricular ejection fraction was 0.27 and 0.37 in patients with and without the events in this study, and 0.20 and 0.28 in the previous study, although the causes of sudden death are unknown.¹²⁾ An index of severity of heart failure may be a useful predictor of future events in tachycardia-induced cardiomyopathy.

Sudden death: Sudden death occurred after normalization of cardiac function in 1 of 12 patients in this study, and this was consistent with a previous study describing 3 cases of sudden death out of 24 patients with tachycardia-induced cardiomyopathy.¹²⁾ Therefore, it is suggested that tachycardia-induced cardiomyopathy may increase the risk of sudden death, while it is unclear whether either ventricular tachyarrhythmia degenerated by supraventricular tachyarrhythmia or acute hemodynamic collapse facilitates sudden death. Recently, the recovery of cardiac dysfunction was also reported in patients with aborted sudden death and supraventricular tachyarrhythmia.¹⁶⁾

Treatment: There was no recurrence of heart failure or sudden death in patients whose tachyarrhythmia was successfully ablated. Similarly, recurrence and sudden death occurred only in patients with atrial fibrillation who had not received

catheter ablation in a previous study.¹²⁾ Uncontrolled tachyarrhythmia with a rapid ventricular rate, especially atrial fibrillation, may be critical for recurrent heart failure as well as sudden death in tachycardia-induced cardiomyopathy. Therefore, complete control of tachyarrhythmia is particularly important for long-term management.

To avoid future critical events, catheter ablation can be the first choice as curative treatment for most causative tachyarrhythmias of tachycardia-induced cardiomyopathy because of a high success rate that exceeds 95%.¹⁷⁾ Recent advances in understanding the mechanism and catheter methods enable the elimination of atrial fibrillation, but the recurrence rate is not still sufficient, and the long-term efficacy and indication are not yet fully understood.¹⁸⁻²⁰⁾ Antiarrhythmic drugs may serve as an alternative treatment modality. Pharmacological therapy for atrial fibrillation/flutter has 2 objectives: rhythm control and rate control. However, the effects of antiarrhythmic drugs on maintenance of sinus rhythm are also insufficient and antiarrhythmic drugs may have unintended adverse effects.^{21,22)} Moreover, we demonstrated a recurrence of heart failure and sudden death during optimized rate-control treatment, suggesting that the efficacy of pharmacological rate control is incomplete to prevent future events. Catheter ablation of the atrioventricular node and pacemaker implantation can promise complete control of heart rate from treatment-refractory supraventricular tachyarrhythmias.^{20,23,24)}

Study limitation: Our study population is small and further studies with larger numbers of patients are necessary to clarify the risk of recurrence of heart failure or sudden death. The duration of time from the tachyarrhythmia onset to development of congestive heart failure was not accurate because tachyarrhythmia onset was defined by symptom. Treatments to control tachyarrhythmias were diverse and not administered systematically. Comparison of the efficacy of each therapy was also difficult to assess. One patient had acute exacerbation of hyperthyroidism when heart failure recurred due to an uncontrolled heart rate of atrial fibrillation. Finally, the etiology in one patient who died suddenly was unknown because an autopsy was not performed.

Conclusions: In tachycardia-induced cardiomyopathy, recurrent heart failure with uncontrollable tachycardias and sudden death were observed during the long-term follow-up. Although cardiac dysfunction is reversible, a substrate for heart failure or fatal arrhythmia may persist, mandating strict control of tachyarrhythmia.

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REFERENCES

1. Packer DL, Bardy GH, Worley SJ, Smith MS, Cobb FR, Coleman RE, *et al.* Tachycardia-induced cardiomyopathy: a reversible form of left ventricular dysfunction. *Am J Cardiol* 1986; 57: 563-70.
2. Cruz FE, Cheriex EC, Smeets JL, *et al.* Reversibility of tachycardia-induced cardiomyopathy after cure of incessant supraventricular tachycardia. *J Am Coll Cardiol* 1990; 16: 739-44.
3. Tomita M, Spinale FG, Crawford FA, Zile MR. Changes in left ventricular volume, mass, and function during the development and regression of supraventricular tachycardia-induced cardiomyopathy. Disparity between recovery of systolic versus diastolic function. *Circulation* 1991; 83: 635-44.
4. Shinbane JS, Wood MA, Jensen DN, Ellenbogen KA, Fitzpatrick AP, Scheinman MM. Tachycardia-induced cardiomyopathy: a review of animal models and clinical studies. *J Am Coll Cardiol* 1997; 29: 709-15. (Review)
5. Umana E, Solares CA, Alpert MA. Tachycardia-induced cardiomyopathy. *Am J Med* 2003; 114: 51-5. (Review)
6. Khasnis A, Jongnarangsin K, Abela G, Veerareddy S, Reddy V, Thakur R. Tachycardia-induced cardiomyopathy: a review of literature. *Pacing Clin Electrophysiol* 2005; 28: 710-21. (Review)
7. Yarlagadda RK, Iwai S, Stein KM, *et al.* Reversal of cardiomyopathy in patients with repetitive monomorphic ventricular ectopy originating from the right ventricular outflow tract. *Circulation* 2005; 112: 1092-7.
8. Grogan M, Smith HC, Gersh BJ, Wood DL. Left ventricular dysfunction due to atrial fibrillation in patients initially believed to have idiopathic dilated cardiomyopathy. *Am J Cardiol* 1992; 69: 1570-3.
9. Rabbani LE, Wang PJ, Couper GL, Friedman PL. Time course of improvement in ventricular function after ablation of incessant automatic atrial tachycardia. *Am Heart J* 1991; 121: 816-9.
10. Kieny JR, Sacrez A, Facello A, *et al.* Increase in radionuclide left ventricular ejection fraction after cardioversion of chronic atrial fibrillation in idiopathic dilated cardiomyopathy. *Eur Heart J* 1992; 13: 1290-5.
11. Gossage A, Braxton J. On auricular fibrillation. *QJM* 1913; 6: 435-40.
12. Nerheim P, Birger-Botkin S, Piracha L, Olshansky B. Heart failure and sudden death in patients with tachycardia-induced cardiomyopathy and recurrent tachycardia. *Circulation* 2004; 110: 247-52.
13. Umana E, Solares CA, Alpert MA. Tachycardia-induced cardiomyopathy. *Am J Med* 2003; 114: 51-5. (Review)
14. Kuramochi Y, Guo X, Sawyer DB, Lim CC. Rapid electrical stimulation induces early activation of kinase signal transduction pathways and apoptosis in adult rat ventricular myocytes. *Exp Physiol* 2006; 91: 773-80.
15. Matsumoto K, Takahashi N, Ishikawa T, *et al.* Evaluation of myocardial glucose metabolism before and after recovery of myocardial function in patients with tachycardia-induced cardiomyopathy. *Pacing Clin Electrophysiol* 2006; 29: 175-80.
16. Brembilla-Perrot B, Marcon O, Chometon F, *et al.* Supraventricular tachyarrhythmia as a cause of sudden cardiac arrest. *J Interv Card Electrophysiol* 2006; 16: 97-104.
17. Blomström-Lundqvist C, Scheinman MM, Aliot EM, *et al.* ACC/AHA/ESC guidelines for the management of patients with supraventricular arrhythmias -- executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Supraventricular Arrhythmias). *Circulation* 2003; 108: 1871-909.
18. Haïssaguerre M, Jais P, Shah DC, *et al.* Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. *N Engl J Med* 1998; 339: 659-66.
19. Chen SA, Hsieh MH, Tai CT, *et al.* Initiation of atrial fibrillation by ectopic beats originating from the pulmonary veins: electrophysiological characteristics, pharmacological responses, and effects of radiofrequency ablation. *Circulation* 1999; 100: 1879-86.
20. Fuster V, Rydén LE, Cannom DS, *et al.* ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: full text: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 guidelines for the management of patients with atrial fibrillation) developed in collaboration with the European Heart Rhythm Association and the Heart Rhythm Society. *Europace* 2006; 8: 651-745.

21. Lafuente-Lafuente C, Mouly S, Longás-Tejero MA, Mahé I, Bergmann JF. Antiarrhythmic drugs for maintaining sinus rhythm after cardioversion of atrial fibrillation: a systematic review of randomized controlled trials. *Arch Intern Med* 2006; 166: 719-28. (Review)
22. Page RL, Roden DM. Drug therapy for atrial fibrillation: where do we go from here? *Nat Rev Drug Discov* 2005; 4: 899-910. (Review)
23. Wood MA, Kay GN, Ellenbogen KA. The North American experience with the Ablate and Pace Trial (APT) for medically refractory atrial fibrillation. *Europace* 1999; 1: 22-5.
24. Weerasooriya R, Davis M, Powell A, *et al.* The Australian Intervention Randomized Control of Rate in Atrial Fibrillation Trial (AIRCRAFT). *J Am Coll Cardiol* 2003; 41: 1697-702.