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REVIEW PAPER

Tachycardia-Induced Cardiomyopathy: Evaluation and Therapeutic Options

Tachycardia-induced cardiomyopathy is caused by sustained rapid ventricular rates and is one of the well-known forms of reversible myocardial dysfunction. The diagnosis is usually made retrospectively after marked improvement in systolic function is noted following control of the heart rate. Physicians should be aware that patients with seemingly idiopathic systolic dysfunction may have tachycardia-induced cardiomyopathy and that controlling the heart rate may result in improvement or even complete restoration of systolic function. Congest Heart Fail. *2010;16:122–126.*

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Congestive heart failure is one of the major causes of hospitalization. Therefore, the search for potentially reversible etiologies of cardiomyopathy is of particular importance (Table). Tachycardia-induced cardiomyopathy (TIC) is caused by sustained rapid ventricular rates and is one of the well-known forms of reversible myocardial dysfunction. First reports that incessant or chronic tachyarrhythmias may cause a reversible deterioration of cardiac function date back to the early 1900s.[1,2] Subsequently, it was demonstrated that TIC occurs in experimental models and also in patients with supraventricular or ventricular tachyarrhythmias.[3]

TIC can be defined as cardiac dysfunction caused by a high and/or irregular ventricular rate that is completely or partially reversible after the normalization of heart rate.[3] Two forms may be distinguished: (1) pure TIC, in which tachycardia is the only identifiable cause of myocardial dysfunction and is present in a healthy heart, and (2) impure TIC, when tachycardia causes the deterioration of cardiac function in the context of structural heart disease.[4]

Case Report

A 63-year-old man presented with progressive dyspnea and leg edema over 2 weeks. He had previous diagnoses of hypertension, hyperlipidemia, and obstructive sleep apnea but was not compliant with therapy. Pulse was rapid and irregular with blood pressure of 150/90 mm Hg and moderate jugular venous distension. No murmurs or gallop sounds were evident. Crackles were heard bilaterally in lower lung fields with moderate pitting pedal edema. Chest radiography revealed mild cardiomegaly and pulmonary venous congestion. Electrocardiography revealed rapid atrial fibrillation with ventricular rate of 140/min, left ventricular (LV) hypertrophy and nonspecific ST-T wave changes. Serial troponin estimation revealed a maximum of 0.4 ng/L, which is borderline for myocardial infarction. Echocardiography revealed a dilated LV with moderate global hypokinesia and ejection fraction (EF) of 30%. Heart failure and atrial fibrillation were addressed with furosemide, enalapril, digoxin, and warfarin. Gradually, metoprolol was increased and home heart rate control was monitored daily by patient diary. The patient did well clinically and in 2 months had spontaneously converted to sinus rhythm. Repeat echocardiography revealed normal LV size and function with EF of 60%, confirming the diagnosis of TIC.

Pathophysiology: Molecular Mechanisms of LV Dysfunction in TIC

Most of our knowledge regarding pathophysiology and morphologic features of TIC are based on a canine heart rapid pacing model, which is a widely accepted model of low-output biventricular failure.[5] Underlying histologic changes are characterized by cardiomyocyte lengthening and hyperplasia, extracellular matrix changes, myocardial fibrosis, myofibril misalignment, loss of sarcomere register, and apoptosis.[3,4] Alterations in cellular and neurohumoral regulation have been described and several factors can contribute to the

Table. Common Causes of Transient or Reversible Cardiomyopathy

Coronary artery disease
Hypertension
Myocarditis
Alcohol
Tachycardia-induced cardiomyopathy
Takotsubo–stress cardiomyopathy
Sepsis
Cardiac arrest and cardioversion
Peripartum cardiomyopathy

evolution of TIC. These include abnormal calcium handling[3,6] and β-adrenergic responsiveness,[6] oxidative stress and injury, angiotensin-converting enzyme gene polymorphism,[7] depletion of myocardial energy stores,[3,4] and myocardial ischemia.[3] The latter is probably the most important mechanism. Abnormalities in subendocardial to subepicardial flow ratios and impaired coronary flow have been found in TIC.[3,4] Short diastolic time, when most coronary perfusion normally occurs; low myocardial perfusion pressure from low diastolic blood pressure; high LV end-diastolic pressure; and increased myocardial oxygen demand may account for the myocardial ischemia observed in TIC despite the absence of obstructive coronary disease.[3,4]

Clinical Features and Diagnostic Approach

TIC may follow any type of chronic cardiac arrhythmia: supraventricular tachyarrhythmias, such as inappropriate sinus tachycardia[8]; atrial fibrillation[9–11]; atrial flutter[9]; automatic atrial tachycardia[6]; atrioventricular (AV) nodal reentry tachycardia[6]; automatic AV junctional tachycardia,[6] accessory pathway tachycardia,[6] and ventricular tachycardia[12,13]; and frequent premature ventricular complexes (PVCs).[14–16] Further, TIC has been reported at any age group, from the fetus to the elderly.[3,4]

The incidence of TIC is unknown; most reports have been small retrospective series or case studies involving mostly patients with atrial fibrillation. In patients with atrial fibrillation, approximately 25% to 50% of those with LV dysfunction in selected studies have some degree of TIC.[10,11] Presumed risk factors include the type, rate, and duration of tachyarrhythmia as well as underlying heart disease.[3,4]

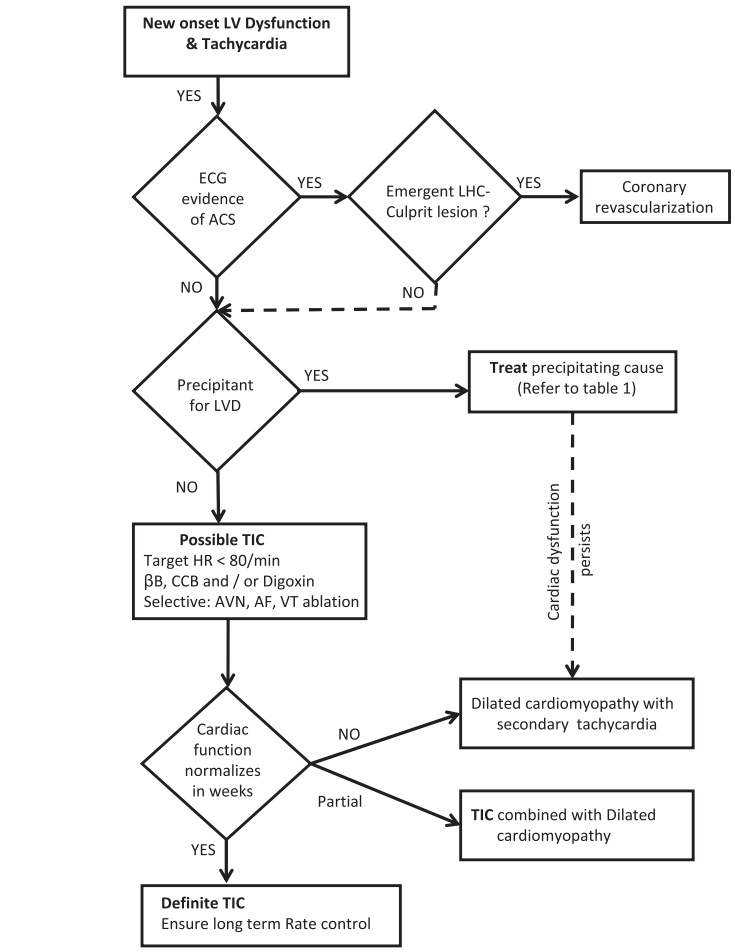

Figure. Clinical presentation–based diagnostic algorithm to limit invasive cardiac testing when tachycardia-induced cardiomyopathy (TIC) is suspected. ACS indicates acute coronary syndrome; AF, atrial fibrillation; AVN, atrioventricular node; βB, β-blockers; CCB, calcium channel blockers; ECG, electrocardiographic; HR, heart rate; LHC, left heart catheterization; LV, left ventricular; LVD, left ventricular dysfunction; VT, ventricular tachycardia.

Unfortunately, there are no diagnostic guidelines for identifying TIC at the initial visit. Therefore, clinicians should suspect TIC when LV systolic dysfunction accompanies persistent tachycardia. The ventricular rate that causes TIC has not been determined, although it is thought that any prolonged heart rate >100 beats per minute may be deleterious.[3,6] The initial evaluation may follow contemporary guidelines for initial evaluation of patients with systolic heart failure.[17] Evaluation of the patient is complicated by the fact that TIC has been reported in structurally normal hearts as well as in various types of structural heart disease.[4,6] Thus, TIC is not excluded by evidence of other forms of structural heart disease, particularly because tachycardia may aggravate already reduced systolic function.[10] Typically, the diagnosis is inferred after observing improvement in ventricular function that follows the control of heart rate. The Figure outlines the overall clinical algorithm for cardiac testing and confirming TIC based on presentation and response to initial therapy.

There are no specific criteria for the diagnosis of TIC, although several facts can be taken into consideration. Data from 2 studies suggested that LV dimen-

sions may be used for differentiation between TIC and dilated cardiomyopathy that is accompanied by supraventricular tachycardia. Fujino and associates[11] performed a retrospective data analysis of 63 patients admitted because of heart failure associated with atrial fibrillation. All patients were identified as not having structural heart disease but had depressed LVEF. Patients were divided into 2 groups: those with rapid (<6 months) normalization of the LVEF after management of atrial fibrillation (presumed TIC, n=30) and those with persistent LV systolic dysfunction (dilated cardiomyopathy, n=33). Although the B-type natriuretic peptide value and LVEF did not differ between the 2 groups, the LV size on admission was significantly smaller in the TIC group—LV end-diastolic dimension (LVEDD) was 57.6±7.2 mm, LV end-systolic dimension (LVESD) was 49.4±8.0 mm—than in the dilated cardiomyopathy group—LVEDD was 63.4±8.8 mm and LVESD was 55.3± 9.6 mm ($P<.05$).

Another study suggests that in patients with LVEF ≤30%, (TIC group, n=12 vs dilated cardiomyopathy group, n=11), LVEDD ≤66 mm could predict TIC with a sensitivity of 100% and a specificity of 83.4%.[9] The reason for the smaller LV cavitary dimensions in TIC is believed to be as follows: Enlargement of the LV is compensatory and time-dependent reflecting gradual disease progression. TIC is believed to be a relatively acute process, limiting the enlargement of the LV. In contrast, dilated cardiomyopathy is believed to be a slowly progressive disease that is latent for a relatively long time before its diagnosis, allowing time for LV enlargement. However, severe dilation of LV does not completely exclude the possibility of TIC.

The imaging approach to TIC will rest on excluding other etiologies for LV dysfunction and establishing the lack of permanent myocardial damage. Echocardiography, being widely available and inexpensive, is the cornerstone in establishing presence of LV dysfunction and narrowing the list of differential diagnoses. Radionuclide imaging can help assess LVEF and detect the presence of myocardial ischemia. Recently, cardiac magnetic resonance (CMR) has been accepted as the gold standard for myocardial tissue characterization.[18] In TIC, one would expect a lack of myocardial infarction or scarring by delayed-enhancement CMR similar to that of stress cardiomyopathy.[19,20] Moreover, CMR can also shed light on alternate etiologies for the cardiomyopathy.[18] Thus, CMR can assume a vital role in management of patients with suspected TIC.

Both nonsustained and sustained ventricular arrhythmia can result in cardiac dysfunction. TIC has been noted in association with idiopathic LV tachycardia[13] and right ventricular outflow tract (RVOT) tachycardia.[12] Bogun and colleagues[16] conclusively demonstrated an inverse relationship between PVC burden and LVEF. According to Bhushan and Asirvatham,[14] features suggesting that PVCs are the primary pathology (and not a secondary finding due to cardiomyopathy) are (1) young healthy patients with no underlying cardiac disease; (2) absence of known coronary artery disease; (3) possibly preserved myocardial thickness and absence of scar on echocardiography; (4) 1 or 2 primary morphologies, suggesting that 1 or 2 localized regions of abnormal myocardium are generating the PVCs rather than widespread myocardial disease that can be expected to give rise to multiple morphologies of PVCs; (5) RVOT, LV outflow tract, or fascicular PVC morphology; and (6) frequent PVCs (often >20,000 beats/day). The latter is not always true, as ectopy-induced cardiomyopathy was reported in patients with only 5500 monomorphic PVCs.[21]

Management of TIC

There is considerable evidence that restoration of a normal heart rate improves LV systolic function and reverses clinical manifestations of heart failure in patients with TIC.[11–14] Thus, the cornerstone in the management of disease in these patients is to achieve normal heart rates. The best means to achieve heart rate control varies depending on the type of arrhythmia.

Atrial Fibrillation

Most of the available data on TIC relates to patients with atrial fibrillation. While restoration of a normal heart rate leads to clinical and hemodynamic improvement, it is less certain whether a strategy of rhythm control is more effective than rate control. Both approaches may be achieved by medical therapy as well as nonpharmacologic means.

Pulmonary Vein Isolation. It is now known that atrial fibrillation is often triggered by ectopic atrial beats originating near the ostia of the pulmonary veins. Ablation of these ectopic foci, or preferably complete electrical isolation of the pulmonary veins, can be achieved either surgically or by radiofrequency (RF) catheter ablation.

Patients with heart failure and cardiomyopathy who have atrial fibrillation may benefit from RF ablation.[22] In this study, a significant improvement of mean LVEF (from 35% to 56%) occurred in patients with heart failure.[22] The greatest improvement was seen within the first 3 months. Among the subset of patients without structural heart disease and with inadequate prior rate control (presumed tachycardia-mediated cardiomyopathy), 92% had a marked improvement in LVEF with ablation (an increase of ≥20% or an increase to a final LVEF of ≥55%).

AV Node Ablation. AV node ablation with ventricular pacing is used in cases of intolerance to drugs or difficulty with rate control. A meta-analysis[23] conducted among 2000 patients who underwent AV node ablation demonstrated improvements in quality of life, cardiac function, and exercise capacity. During the first months after the procedure, a more pronounced increase in LVEF was observed among patients with LVEF <45%. This may be the consequence of the regression of "tachycardiomyopathy" induced by atrial fibrillation as well as the suspension of negatively inotropic drugs and an increase in the ventricular filling time.

In a case of AV ablation the choice of pacemaker may be important, as

more physiologic biventricular pacing was found to be superior to right ventricular pacing.[24] Furthermore, even in the absence of cardiomyopathy, chronic right ventricular pacing may result in myocardial perfusion defects, regional wall motion abnormalities, and adverse hemodynamics.[25]

AV Node Ablation vs Pulmonic Vein Isolation. The relative efficacy of AV node ablation with biventricular pacing for rate control and pulmonary vein isolation for rhythm control was compared in a prospective randomized trial of 81 patients with New York Heart Association class II or III heart failure who had symptomatic drug-refractory atrial fibrillation.[26] At 6 months, pulmonary vein isolation was associated with statistically significant improvements in LVEF (35% vs 28%), 6-min walk distance (340 vs 297 m), and score on the Minnesota Living With Heart Failure questionnaire. Moreover, approximately 30% of patients treated with AV node ablation and biventricular pacing had progressive atrial fibrillation (eg, paroxysmal to persistent atrial fibrillation), which was not seen in pulmonary vein isolation patients.

Ventricular Arrhythmias

When TIC is caused by idiopathic ventricular arrhythmias (PVCs, idiopathic LV tachycardia, RVOT tachycardia) the reversal of cardiac dysfunction may be achieved by means of medical therapy or ablation. Because of myocardial dysfunction, the choice of antiarrhythmic therapy options is limited. Class IA and IC agents are contraindicated because of malignant proarrhythmia in the setting of myocardial dysfunction.[17] Class IV agents known to adversely affect the clinical status of patients with current or prior symptoms of heart failure and reduced LVEF should be avoided or withdrawn whenever possible.[17] An exception to this rule is amiodarone, but its noncardiac side effects preclude long-term use, particularly in younger patients. As a result of these difficulties and the fact that the myocardium responsible for idiopathic ventricular arrhythmias is often highly localized, RF ablation is employed as an effective and often curative therapy for these arrhythmias.[12,13,16,27] At the time of the ablation procedure, it is often not clear whether the frequent arrhythmias are causing LV dysfunction. To assess the contribution of dysrhythmia to ventricular dysfunction, pharmacologic suppression, such as by amiodarone therapy, may be considered, but the utility of this approach and duration of therapy required have not been defined.[27] Multiple morphologies of PVCs or ventricular tachycardia are likely to reduce procedural success. In the absence of a predominant PVC morphology, medical management may be superior.[27]

TIC in Children

In the pediatric population, supraventricular tachycardia is the most common tachyarrhythmia, which at times is incessant leading to the development of TIC and presenting as heart failure.[28] Short-term amiodarone in combination with digoxin and/or propranolol is reported to be safe and effective for treatment of infants and children with "tachycardiomyopathy." Control of tachycardia is achieved in the majority, leading to recovery of ventricular function.[29] In cases of drug refractoriness, RF catheter ablation has proven effective in managing various forms of supraventricular tachycardia and therefore TIC.[28]

Follow-Up

Patients with a history of successfully treated TIC are susceptible to a more severe cardiomyopathy if the offending tachyarrhythmia recurs, and they are also at risk for sudden death.[30,31] Clinical, electrocardiographic, and echocardiographic surveillance for recurrence of TIC would be driven by initial success with antiarrhythmic therapy, compliance with medications, and progression of symptoms. It was shown that patients with TIC continue to have persistent negative LV remodeling (increased LVESD and LV end-diastolic and end-systolic volumes) even after their EF and heart rate have normalized with appropriate treatment. Therefore, patients with TIC and improved LVEFs may need to be treated long-term with pharmacotherapy such as β-blockers and angiotensin-converting enzyme inhibitors that have been shown to reverse remodeling and decrease mortality in patients with LV systolic dysfunction.[32]

Conclusions

TIC is a reversible form of cardiomyopathy and heart failure caused by supraventricular and ventricular tachyarrhythmias. Its diagnosis requires a high index of suspicion, and the physician dealing with heart failure patients should always consider the possibility of TIC when patients have a chronic arrhythmia and should always adequately treat these chronic arrhythmias. The latter may result in improvement or even complete normalization of systolic function.

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