Tachycardia induced Cardiomyopathy

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Tachycardiomyopathy is an uncommon, however well recognized entity caused by long standing tachycardia which is usually treatable, reversible and hence have good prognosis.

Tachycardiomyopathy is reported and seen with all type of tachyarrhythmias. Supraventricular arrhythmias such as atrial fibrillation, atrial flutter, atrial tachycardias and reentrant supraventricular tachycardia (SVT) can lead to tachycardiomyopathy. Ventricular arrhythmias rarely lead to tachycardiomyopathy since this arrhythmia is usually associated with some form of underlying structural heart disease. However, idiopathic left ventricular tachycardia (ILVT) or right ventricular outflow tract VT can arise in structurally normal hearts. In rare cases, these arrhythmias are persistent or repetitive enough to result in a cardiomyopathy.
Tachycardiomyopathy termed was first coined by Gallagher JJ. Fenelon et al described two varieties of tachycardiomyopathy. One as ‘pure type’ and other as ‘impure type’. In pure type chronic tachycardia cause LV dysfunction and it completely recovers after tachycardia is terminated. In impure form, cardiac function may not recover incompletely as it occurs in patients with structural heart disease. Chronic tachycardia ultimately leads to left ventricular dilatation and cellular morphologic changes.

Many alterations in neurohumoral and cellular activation have been described, and several factors probably contribute to the development of rate-related myocardial dysfunction. These factors are depletion of myocardial energy stores and myocardial ischemia, abnormal calcium handling and beta-adrenergic responsiveness, oxidative stress and injury.

Clinically ectopic atria tachycardia and PJRT accounts for the most of the causes of tachycardiomyopathy in children. Atrial fibrillation and atrial flutter also leads to tachycardiomyopathy if ventricular rates are not controlled. However, there is an association between heart failure and atrial fibrillation. Multiple times it not possible to determine which is causative. Around 25 to 50 percent of patients with LV dysfunction and AF have some component of arrhythmia-induced cardiomyopathy.

Ventricular arrhythmias rarely account for tachycardiomyopathy, as this is usually associated with structural heart disease. However, idiopathic left ventricular tachycardia or right ventricular outflow tract VT can arise in structurally normal hearts. Rarely, these arrhythmias are persistent or repetitive enough to result in a cardiomyopathy. Frequent ventricular premature complexes (PVC) defined as greater than 10 percent of overall heartbeats in the form of VPCs have been associated with a reversible cardiomyopathy.

Baman et al. proposed a PVC burden of >24% as independently associated with PVC-induced cardiomyopathy (sensitivity 79%, specificity 78%). The lowest PVC burden resulting in cardiomyopathy was found to be 10%. Atrial premature complexes (APCs) are usually benign, but a high burden of APCs can lead to cardiomyopathy. The basic of management of tachycardiomyopathy is controlling heart rate by pharmacological and non-pharmacological approaches.

The initial treatments for a patient suspected tachycardiomyopathy are same as those as in patients with heart failure with reduced ejection fraction (e.g., angiotensin converting enzyme [ACE] inhibitors or angiotensin receptor blockers [ARBs], beta blockers, ivabradine, angiotensin receptor - nepritisyn inhibitor and diuretics) and tachyarrhythmias (e.g., rate-control medications, consideration of antiarrhythmic drugs and/or cardioversion). Jeong YH et al showed that strategy of rate control as effective as rhythm control for ejection fraction improvement and prognosis in patients with tachycardiomyopathy.

For atrial fibrillation and flutter induced suspected tachycardiomyopathy heart rate control through either means (rate control or rhythm control) can be effective at improving cardiac function. B-blockers, digitalis, non-dihydropyridine calcium channel inhibitors, or combinations are widely used for rate control. Rate control strategy is considered to be non-inferior to rhythm control, as long as that heart rate does remain controlled, except in symptomatic patients as shown in AFFIRM trial.

In pediatric age group, EAT or PJRT are often incessant. As also seen in our case. Amiodarone is the commonly used drug for patients with LV dysfunction and tachyarrhythmias. Juneja et al reported successful use of amiodarone in combination with digoxin/propranolol as safe and effective treatment strategy for infants/children with tachycardiomyopathy. There are case reports of successful treatment of PJRT with amiodarone in neonatal period. Similarly, complete resolution of ventricular tachycardia induced cardiomyopathy by oral amiodarone has also been reported.
Radiofrequency (RF) ablation can be used successfully for the treatment of tachyarrhythmia:

Almost all arrhythmias such as EAT, PSVT, PJRT, atrial fibrillation/flutter, frequent premature ventricular extra systole, and ventricular tachycardia can be successfully ablated (Figure) and leads to improvement and even normalization of left ventricular function. Balbir Singh et al reported successful reversibility of left ventricular function after RFA of incessant idiopathic left ventricular tachycardia. Hence, there is a school of thought that catheter ablation in patients with tachycardiomyopathy should be considered as the first-line therapy as soon as possible. Surgical therapy is also an option for these patients. Rabbani et al reported a case of tachycardiomyopathy due to EAT which underwent surgical cryoablation. LV function improved one month after the operation.

In conclusion, tachycardiomyopathy is treatable cause of left ventricular dysfunction with good prognosis. The diagnosis of tachycardiomyopathy is not straight forward, but if these patients are adequately treated either pharmacologically or by catheter ablation will have significant improvement and even normalization of left ventricular ejection fraction.

Figure. Termination of tachycardia occurred within 5 seconds of radiofrequency burn in a fourteen-year-old girl diagnosis of dilated cardiomyopathy. Earliest A was mapped at inferior rim of CS os.
Hypertrophic cardiomyopathy (HCM) is the most relevant structural genetic heart disease. It is diagnosed in 1 out of 500 individuals in the general population. It is most characteristic phenotype displays an asymmetric septal hypertrophy, predominantly in its proximal portion, causing some tethering effect in the subvalvular apparatus of the anterior leaflet during the left ventricular ejection, producing a dynamic obstruction of the left ventricular outflow tract and an eventual mitral regurgitation. Some patients are asymptomatic and even participate in highly competitive sports and their condition is occasionally suspected fortuitously by the presence of a murmur or an EKG finding of left ventricular hypertrophy or an abnormal echocardiogram. Other less common phenotypes include generalized ventricular hypertrophy, apical hypertrophy, or free wall hypertrophy. Once having established the diagnosis of HCM the threat of sudden death will come to consideration. In the earlier series, the risk of sudden death seemed to be much higher than in the most recent ones, probably because of selecting the worst cases that were referred to specialized clinics. Currently it is estimated to be in general around 1% per year. The occurrence of sudden death has been observed in all ages but it is largely most common among the young.

Figure 1. Death rate and mode of death in HCM.

Adapted from Maron B et al. Epidemiology of Hypertrophic Cardiomyopathy-Related Death Circulation 2000;102:858-864.
There is abundant documentation of ventricular arrhythmias as the mechanism of sudden death in the majority of cases, as could be seen during Holter monitoring demonstrating ventricular tachycardia and fibrillation in such cases.

Histopathologic findings in myocardial biopsy and in autopsy clearly show, in addition to the hypertrophy, a characteristic fiber disarray in the midst of variable degree of fibrosis that set the proper stage for the development of sites for microreentry. The thought of ventricular arrhythmias as the likely cause of the sudden death brings to mind the use of implantable cardioversion-defibrillator (ICD) as a therapeutic option to prevent this occurrence. And, as a matter of fact, ICDs have been efficaciously utilized with that aim in patients with HCM. However, we should have means of discriminating those patients that would benefit the most from the use of this resource.

**THE CHOOSING OF THE RIGHT HCM PATIENT FOR THE USE OF AN ICD:**
In secondary prevention, that is, in patients surviving from a cardiac arrest or with documented ventricular tachycardia, the ICD indication is quite established as it has been shown to act in a significant number of episodes that would presumably lead to sudden death, and that proves to be rather frequent in this condition.

Therefore patients who have been resuscitated from a cardiac arrest or in those in whom the presence in a Holter monitor of a ventricular tachycardia with a duration longer than 30 beats and with a rate greater than 120 bpm, are unquestionable candidates for the ICD implantation.

The other situation in which ICDs are used in HCM is for primary prevention, that is, in patients considered as a high risk for sudden death, but have not yet experienced the situation mentioned above, that is, neither a cardiac arrest nor a sustained life-threatening VT.

Cohort studies have shown the prediction capacity of these individual risk factors for sudden death in HCM as explicated in Table I.

**Table I - Prediction of sudden death.**

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Hazard ratio (95% CI)</th>
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<tr>
<td>Septal thickness &gt; 30mm</td>
<td>3.10 (1.81 - 4.40)</td>
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<tr>
<td>NSVT</td>
<td>2.89 (2.21 - 3.58)</td>
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<tr>
<td>Unexplained syncope</td>
<td>2.68 (0.97 - 4.38)</td>
</tr>
<tr>
<td>Family history of sudden death</td>
<td>1.27 (1.16 - 1.38)</td>
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On the other hand, a linearity has been recognized between septal thickness and sudden death occurrence, and thus, a dichotomized situation of septal thickness greater or lesser of 30mm might not be sufficient for a decision regarding implantation of an ICD in a certain HCM patient. Besides, the individual presence of each one of these risk factors in patients who had sudden death varies from 9 to 30%.

A recent score was built by the European Society of Cardiology, the Risk Score for Sudden Death in HCM - (HCM Risk-SCD), that established a prognostic score analyzing retrospectively 6 distinct cohorts in 6 European centers comprising a total of 3066 cases of HCM, with a median of 5.7 years of follow-up, which included 198 cases of documented sudden deaths among them.

The risk factors that were identified were age (years), maximal septal thickness (mm), left atrial diameter (mm) maximum left ventricular outflow tract gradient (mmHg), family history of sudden death, NSVT in a 24 h Holter and a history of unexplained syncope.
These factors were submitted to an univariate analysis and those with a coefficient of contribution was greater than 15% were proceeded to the multivariate analysis.

An online calculator was thus but which predicts the 5 years risk for sudden death in the HCM population: www.HCMRisk.org, http://www.doc2do.com/hcm/webHCM.html

This calculation will help in choosing the patient with HCM that will benefit from an ICD as is shown in Table II.

<table>
<thead>
<tr>
<th>Low risk (&lt; 4%)</th>
<th>Intermediate risk (4 e &lt;6%)</th>
<th>High risk (&gt;6%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICD not indicated</td>
<td>ICD could be considered.</td>
<td>ICD is indicated.</td>
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This score was validated in another European population of 706 patients in a follow up longer than 7 years, demonstrating a predication by C statistic of 0.69, which proved to be superior to the 2003 ACC/ESC guideline of 0.55 and the 2011 ACCF/AHA guideline of 0.60.6

CARDIAC NUCLEAR MAGNETIC RESONANCE (CNMR) AND RISK STRATIFICATION FOR SUDDEN DEATH IN PATIENTS WITH HCM.

Despite the appreciated contribution of the scores for sudden death prediction in HCM patients, they still lack the desirable accuracy. In addition to this, there has been some questioning regarding the HCM Risk-SCD hability to predict sudden death occurrence in series of patients seen in HCM specialized clinics in the USA. With the advent of CNMR and its capacity of detecting fibrosis, which was proven of value in establishing prognosis in ischemic cardiomyopathy, the attention has turned to its application in risk stratification in HCM. Rochite et al. in Brasil, were among the first to point toward its potential role.

Figure 2. Fibrosis prevalence in HCM sudden death patients.

Figure 3. Relation between extent of gadolinium enhancement (LGE) and sudden cardiac death (SCD) events in 1293 patients with hypertrophic cardiomyopathy. A, Hazard plot based on multivariable Cox regression analysis (P=0.008). B, Incidence of SCD events increased progressively and in direct relation to the extent of LGE (P<0.001).
Prevalence of myocardial fibrosis and other classic risk factors for sudden death in hypertrophic cardiomyopathy patients with ICD who present high risk for sudden death with an emphasis on the observation that this risk was substantial when the amount of fibrosis exceeded 1%.

Figure 4. Distinct patterns of myocardial fibrosis in HOCM.

At the present moment this information provided by the CNMR has been considered as potentially useful both to increment the ICD indication for those patients with a low score as well as to refrain from its indication in the patients with greater risk score and small amount of fibrosis. Although the latter has been more subjected to questioning. In any way, one can easily foresee a progressively more important contribution of CNMR in the ICD indication in HCM patients, as it should be seen in next guidelines regarding this condition.

CONCLUSION:
Despite of its low occurrence there is a recognized threat of sudden death in patients with HCM. The adequate utilization of an ICD represents the most efficacious therapy to its prevention.

The correct choice of the patient that will benefit most from this expensive and occasionally troublesome resource depends on the precise definition of the candidate. There is not much discussion when dealing with a secondary prevention. But, in the primary prevention setting the need to best select the patient, considering it’s still a slightly imprecise method of identification, a matter that needs continued development. For the moment, we feel that the HCM Risk-SCD is useful and have great hope that the CNMR will help to refine this decision.
Heart failure (HF) is a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood. Heart failure is severe end stages of many cardiovascular diseases. Epidemiological studies on heart failure have focused mainly on the prevalence, incidence, mortality, fatality, and the distribution and temporal trends of these indicators among different populations. A published review from China to highlight important epidemiological studies of heart failure in China.

Prevalence
The prevalence of HF refers to the rate of the patients with a HF in the specific population at the time of investigation. The Chinese Multicenter Cooperation study on Cardiovascular Health was the first national investigation of chronic HF prevalence in China; enrolled 15,518 adults aged 35-74 years from 10 provinces using a four-stage random-sampling method. The prevalence rates of chronic HF were 0.9%, 0.7% and 1.0% for the overall population, males, and females, respectively. When stratified by age, the prevalence rates of chronic HF were 0.4%, 1.0%, 1.3%, and 1.3% for groups aged 35-44, 45-54, 55-64, and 65-74 years, respectively. Another large-scale study of regional chronic HF prevalence investigated epidemiologic characteristics and treatment of chronic HF in rural areas of Liaoning province in north China.

Using cluster random sampling, 33,027 rural residents aged 25-95 years were recruited. The study reported that the rates of chronic HF prevalence were 1.61%, 0.95%, and 2.28% in the overall, male, and female populations; the prevalence of chronic HF in females was substantially higher than that of males in every age group.

Incidence
The incidence of HF refers to the rate of new HF cases occurring during a certain time period (generally one year) in the population at risk.

In China, the only study [5] reporting the incidence of HF was the above-mentioned study in Hong Kong. Among the 6,203 patients admitted from 11 hospitals, 4,589 were new cases. The incidence of HF was about 0.07% (number of new cases divided by the population of Hong Kong that year) and, when stratified by age groups, showed a rising trend with age. In the > 85-year age group, the incidence for females was 2% and for males was 1.4%.

Changes in original disease of HF
In the 1980s, almost 50% of HF cases were attributable to rheumatic heart disease (RHD), but the HF resulted from RHD has declined significantly in the past three decades. Coronary heart disease has become the main cause of HF in China. A retrospective investigation of hospitalized patients with HF in some parts of China in 1980, 1990, and 2000 analyzed the data of patients with primary diagnoses of chronic HF from 42 hospitals in different cities in China. The study demonstrated that common causes of HF were coronary heart diseases, rheumatic valvular heart disease, and hypertension. From 1980 to 2000, the HF from coronary heart disease rose from 36.8% to 45.6%; A pilot survey of the main causes of chronic HF in patients treated in 2066 primary hospitals in China The research showed that the top three main causes of chronic HF were coronary heart disease (57.1%), hypertension (30.4%), and rheumatic heart disease (29.6%).
Medical therapy
The survey of medical therapies by Cao et al showed that current chronic HF medications used in primary hospitals in China were not optimal. The usage rates of target doses of β-blocker and ACEI were very low (1% and 2%, respectively) and, in some underdeveloped areas (e.g., Qinghai and Guizhou), the use rates were zero.

The investigation of epidemiologic characteristics and treatment of chronic HF in some rural areas of Liaoning province [4] demonstrated that traditional Chinese medicine was widely used in this rural area but that the administration of recommended medicine was very limited. The drugs used were digoxin (6.8%), furosemide (2.45%), hydrochlorothiazide (1.69%), spironolactone (0.38%), ACEI (4.33%), β-blocker (3.77%), and nitrate (3.77%).

An investigation of the prevalence and related factors of medicinal therapy in patients with chronic systolic HF was carried out by Yu et al. Data on 16,681 patients hospitalized with chronic systolic HF were taken from 12 tertiary hospitals in eight cities of Hubei province in 2000 and 2010. Analysis determined the usage rates of β-blockers (46.58%), ACEIs (51.60%), ARBs (18.68%), digitalis (46.24%), and diuretics (69.13%).

Conclusions
HF is becoming more prevalent in China, especially in older people. This results in increasing medical costs and rates of disability and mortality. The underlying disease for HF has changed from RHF to CHD. There were recognized gap between the evidence-based recommendations from the clinical guidelines of HF management and the clinical practice in China.

The Comparison of 2016 ACC/AHA/HFSA and ESC Guidelines Recommendations for Chronic Heart Failure Management

Chronic heart failure (CHF) is a global epidemic of the twenty-first century, affecting millions of patients worldwide. Although important progress has been made in the management of heart failure (HF), morbidity and mortality remains high. Both the ESC and the ACC/AHA/HFSA committees have published HF management guideline in 2016. In this article, will discuss the main differences between the two guidelines and highlight what is new in the management of CHF.

While the ESC 2016 guideline is a full revision of prior HF guideline, ACC/AHA/HFSA guideline is a focused update of 2013 only marking what is new (Table 1). Both guidelines have incorporated new therapies for CHF. There are two new medications derived from the studies PARADIGM-HF trial and SHIFT-HF trial. Also, the ESC guideline has mentioned a new terminology for patients with HF, new recommendations on prevention of CHF and modified the indications for cardiac resynchronization therapy (CRT) implantation.
A new therapeutic algorithm for treatment of patients with HFrEF is recommended in the ESC 2016 guideline. An angiotensin receptor neprilysin inhibitor (ARNI), sacubitril/valsartan is indicated as a replacement therapy for an ACE inhibitor to further reduce the risk of HF hospitalization and death in ambulatory patients who remain symptomatic despite optimal treatment with an ACE-inhibitor, a B-blocker and a mineralocorticoid-receptor antagonist.

Both guidelines established the use of ARNI as a Class IB indicated therapy but the American society emphasizes that only one randomized clinical trial, PARADIGM-HF took place, by giving a level of evidence “B-R”. There is another slight difference between the two guidelines as AHA/ACC/HFSA guideline states “in patients with chronic symptomatic HFrEF NYHA class II-III who tolerate an ACE-inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality”.

The ESC guideline recommendation is more dependent on the study design. Both guidelines emphasize the importance to stop taking ACE inhibitor 36 hours before switching to ARNI. Both guidelines recommend the use of ARNI as replacement for an ACE-inhibitor, but clinical experience will provide further information about the use of ARNI. Will it become first line therapy in the future?

The 2016 ESC guideline have implicated a new term - HF with midrange ejection fraction (HFmrEF) - to classify patients with HF and LVEF of 40-49%. There are clear recommendations for patient’s treatment with HF with reduced ejection fraction (HFrEF), which requires a LVEF of less than 40% and HF with preserved ejection fraction (HFP EF), which requires a LVEF of ≥50%.

The ESC HF Guideline in 2012 defined LVEF 40-49% as “grey area” and with the new guideline we have a new group, HFmrEF that we will need to find new ways of treatment. The “grey area” has always been a matter and the American society mentioned this group as an intermediate group in 2013 HF guideline. By giving a new name “HFmrEF”, have we really created a new population? What will this change in daily practice? Further studies will be needed to improve our understanding of pathophysiology and management of this group. There are recommendations on delaying or preventing the overt HF or preventing death before the onset of symptoms in the ESC 2016 guideline. In patients with asymptomatic CHF treatment of arterial hypertension, statin use in patients with or at high risk of coronary artery disease, use of ACE-inhibitor and B-blockers in patients with a history of myocardial infarction is recommended in preventing or delaying the onset of HF and prolong life. Also, a new hypoglycaemic drug empagliflozin, (an inhibitor of sodium-glucose co-transporter 2) has been shown to improve outcomes in patients with type 2 diabetes and is recommended as Class IIA with a level of evidence B to be used in order to prevent or delay the onset of HF and prolong life.
Ivabradine, sinoatrial node modulatory was first pronounced in 2012 ESC HF guideline. Today both guidelines recommend the use of ivabradine in patients with HFrEF in sinus rhythm, with a heart rate \(\geq 70\) bpm, who are receiving optimal medical therapy with a maximum tolerated dose of B-blocker.

Recommendations for CRT implantation in patients with CHF have been modified in the ESC 2016 guideline. CRT implantation is now contraindicated in patients with HFrEF and QRS duration <130 ms. Class I A recommendation is for symptomatic patients with HF in sinus rhythm with a QRS duration \(\geq 150\) ms and left bundle branch block (LBBB) QRS morphology, with LVEF \(\leq 35\%\) despite optimal medical therapy. Patients with QRS duration of 130-149 ms and LBBB QRS morphology received a Class IB recommendation, where else the indications for other patients with HFrEF and QRS duration \(\geq 130\) ms received a lower class of recommendation.

### Table 1. Comparison of changes in heart failure management guidelines in 2016

<table>
<thead>
<tr>
<th>ESC Guideline</th>
<th>ACC/AHA/HFSA Guideline Update</th>
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<td>- Terminology of HF; introducing a new term; HFmrEF</td>
<td>- New pharmacological therapy for HF.</td>
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| - Delaying or preventing the development of overt HF or preventing death before the onset of symptoms | - ARNI: in patients with chronic symptomatic HFrEF NYHA class II-III who tolerate an ACE-inhibitor or ARB, replacement by an ARNI is recommended to further reduce morbidity and mortality.  
  *Class I, Level B-R* |
| - New therapeutic algorithm for patients with symptomatic HFrEF.  
  - ARNI: Sacubitril/valsartan is recommended as a replacement for an ACE-I to further reduce the risk of HF hospitalization and death in ambulatory patients with HFrEF who remain symptomatic despite optimal treatment with an ACE-I, a beta-blocker and an MRA. *Class I, Level B* |
| - Modified recommendations for CRT implantation in patients with HF | - Ivabradine: Can be beneficial to reduce HF hospitalization for patients with symptomatic stable chronic HFrEF (LVEF \(\leq 35\%\)) who are receiving GDEM, including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a heart rate of 70 bpm or greater at rest. *Class IIa, Level B-R* |

ACE: angiotensin-converting enzyme; ARB: angiotensin-receptor blocker; ARNI: angiotensin receptor-neprilysin inhibitor; CRT: cardiac resynchronization therapy; HF: heart failure; HFmrEF: heart failure with mid range ejection fraction; HFrEF: heart failure reduced ejection fraction.

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