Clinical Practice Guideline

Heart Failure Council of Thailand (HFCT) 2019 Heart Failure Guideline: Sudden Cardiac Death and Device Therapy in Heart Failure

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Prevalence

Ventricular arrhythmias (VAs) range in severity from premature ventricular contraction (PVC) to life-threatening ventricular tachycardia (VT) and ventricular fibrillation (VF). VAs are especially common in patients with ischemic etiology, and in those with lower left ventricular ejection fraction (LVEF)[1]. VAs is an important, widely recognized, and well-established cause of sudden cardiac death (SCD). SCD is defined as an electrical disturbance that causes the heart to malfunction and stop pumping blood to the rest of the body. Concurrent comorbidities, such as coronary artery disease (CAD) and obstructive sleep apnea (OSA) can contribute to the onset of SCD. A sub-analysis of data from the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) trial found rapid-rate non-sustained ventricular tachycardia (NSVT) in HF patients to be significantly associated with appropriate implantable cardioverter defibrillator (ICD) therapy and all-cause mortality[2].

The early drug trials in heart failure (HF) [Studies of Left Ventricular Dysfunction (SOLVD), Vasodilator Heart Failure Trial (V-HeFT) I and II, Prospective Randomized Milrinone Survival Evaluation (PROMISE), and Grupo de Estudio de la Sobrevida en la Insuficiencia Cardiaca en Argentina (GESICA)] reported a prevalence of NSVT ranging from 30% to 60%, with little difference between New York Heart Association (NYHA) Class II and III HF. The most recent survey in an Asian population from a national health insurance database that covers the entire population of Taiwan and that analyzed 7,894 patients aged 40 years or over that were hospitalized for HF, but with no prior VT/VF/SCD or ICD, revealed that new-onset VT/VF/SCD as a combined endpoint occurred in 567 patients (7.2% or 1.95% per annum)[3].

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Impact

Fifty percent of all deaths in advanced HF are sudden and presumed due to VT/VF[4]. A large 5,517 patient outpatient registry of HF reported VT/VF to be associated with increased risk of mortality [hazard ratio (HR) 1.70, 95% confidence interval (CI) 1.41 to 2.05) and sudden death (HR 1.58, 95% CI 1.21 to 2.06) over a 1-year follow-up period[5]. The same study found VT (episode of more than three beats from 24-hour Holter) to be an independent predictor of both total mortality (HR 1.76, 95% CI 1.28 to 2.42) and sudden death (HR 1.96, 95% CI 1.25 to 3.08) at one year. In the Sudden Cardiac Death in

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Table 1. Screening for arrhythmia

Clinical setting	Monitoring suggestion
Stable HF	Rhythm monitoring (e.g., AF, PVC, and NSVT by ECG during OPD visit)
Asymptomatic post-MI and LVEF 30% to 40%	Detection of arrhythmia from ECG, and risk stratification by EPS if NSVT was documented
Symptoms suggestive of arrhythmia	Investigate according to correlated symptoms, such as ECG and Holter monitor
Syncope	Evaluate SCD risk by ECG, Holter monitor, and EPS

AF=atrial fibrillation; ECG=electrocardiogram; EPS=electrophysiology study; HF=heart failure; LVEF=left ventricular ejection fraction; MI=myocardial infarction; NSVT=non sustain ventricular tachycardia; PVC=premature ventricular contraction; SCD=sudden cardiac death

Heart Failure Trial (SCD-HeFT)[6], deaths occurred in 182 of 829 (22.0%) subjects randomized to receive an ICD, in 240 of 845 (28.4%) subjects randomized to the amiodarone group, and in 244 of 847 (28.8%) subjects randomized to the placebo group. Ventricular tachyarrhythmic death occurred in only 37 (4.5%) subjects in the ICD group, in 75 subjects (8.9%) in the amiodarone group, and in 95 subjects (11.2%) in the placebo group.

Pathophysiology

Ventricular arrhythmias occurred from several mechanisms as a result of various types of remodelling. Remodeling in this setting takes the form of molecular changes in electrical, structural, metabolic, and contractile variables to preserve adequate cardiac function.

The triggers of arrhythmias, such as mechanical stretch (volume), neurohormonal activation, and other triggers (e.g., inflammation), should be further investigated.

Recommendations for monitoring arrhythmia (Table 1)

All patients with heart failure should be screened for arrhythmia by physical examination that focuses on rhythm abnormalities, and heart rate should be checked for at least one minute by auscultation and pulse palpation. Further investigations are hereafter described.

Management of ventricular arrhythmia

Therapy with HF medications

In all HF patients presenting with VT, optimization of standard HF therapy with angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs), beta-blocker, and mineralocorticoid receptor antagonist (MRA) is recommended (Class I, level A indication). The need for revascularization should be considered in patients with known or suspected ischemic heart disease and ventricular tachycardia.

Therapy with anti-arrhythmic drugs (Table 2, 3)

Beta-blockers remain the mainstay treatment in heart failure therapy, with well-documented ability to reduce total mortality by 35%, and a 40% to 45% reduction in SCD.

Device therapy

Implantable cardioverter defibrillator (ICD)

It is well established that ICDs reduce mortality by 20% to 24% over a 2-year to 5-year follow-up period in patients with HFpEF or HFrEF with previous cardiac arrest or documented VF or sustained VT, or with syncope and clinical VT (secondary prevention).

A meta-analysis showed a significant reduction in death from any cause with ICD therapy, with a hazard ratio (ICD: amiodarone) of 0.72 (95% CI 0.60 to 0.87; $p<0.0006$), or the outcome of arrhythmic death, with a hazard ratio of 0.50 (95% CI 0.37 to 0.67; $p<0.0001$)[7]. Patients with HF who develop sustained ventricular tachyarrhythmia (either sustained monomorphic or polymorphic VT, VF, or recurrent syncope with inducible sustained VT at the electrophysiological study) are candidates for ICD implantation, as long as they have a life expectancy of more than one year (Table 4).

Cardiac resynchronization therapy (CRT)

Various CRT studies reported that among patients having an indication for an ICD, a cardiac resynchronization therapy defibrillator (CRT-D) device is recommended in those also having HF symptoms of NYHA Class II, III, or ambulatory IV, an LVEF of 35% or less, and a QRS duration of 120 ms or more (Table 5, 6). To ensure effective CRT with more than 95% ventricular pacing, care must be taken to check

Table 2. Recommendations regarding the treatment of ventricular arrhythmia with antiarrhythmic agents

Recommendation	COR	LOE
Beta-blocker (approved agents are bisoprolol, carvedilol, metoprolol succinate, and nebivolol) is recommended in all heart failure patients to prevent ventricular arrhythmia, unless contraindicated.	I	A
Amiodarone can be used to reduce the number of events as adjunct therapy to ICD.	IIa	B
Sotalol can be used as adjunct therapy to ICD to reduce the number of events, but with slightly increased risk of Torsade de Pointes.	IIb	C
Dronedarone, flecainide, and propafenone should not be used to treat ventricular arrhythmia in HF patients.	III	A

COR=class of recommendation; HF=heart failure; LOE=level of evidence; ICD=implantable cardioverter defibrillator

Table 3. Recommendations regarding the treatment of PVC

Recommendation	COR	LOE
Beta-blocker is recommended in symptomatic and high-burden (>10,000/24 hours) with LV systolic dysfunction.	I	A
Asymptomatic PVC with low-burden (<10,000/24 hours) can be re-evaluated and reassured periodically every 3 to 6 months.	I	B
Amiodarone or catheter ablation of PVC can be considered after failure of beta-blocker therapy.	IIa	C
Amiodarone should not be used in asymptomatic PVC.	III	C

COR=class of recommendation; LOE=level of evidence; LV=left ventricle; PVC=premature ventricular contraction

Table 4. Recommended indications for ICD in patients with HF

Recommendation	COR	LOE
ICD therapy is recommended in patients with symptomatic HF (NYHA Class II-III) and LVEF ≤35% after ≥3 months of guideline-directed medical therapy to reduce SCD who are expected to survive for at least 1 year with good functional status:	I	
• Ischemic etiology (at least 6 weeks after myocardial infarction)		A
• Non-ischemic etiology		B
ICD therapy is recommended in patients who develop sustained ventricular tachyarrhythmia (either sustained monomorphic or polymorphic VT, VF, or recurrent syncope with inducible sustained VT at the electrophysiological study) to reduce SCD.	I	A
ICD implantation should be considered for primary and secondary prevention of SCD in patients who are waitlisted for heart transplant.	IIa	A
ICD is not recommended in patients who have a life expectancy less than 1 year.	III	A

COR=class of recommendation; ICD=implantable cardioverter defibrillator; LOE=level of evidence; LVEF=left ventricular ejection fraction; NYHA=New York Heart Association; SCD=sudden cardiac death; VF=ventricular fibrillation; VT=ventricular tachycardia

when to interrogate the device. Sipahi et al performed a meta-analysis of 33 clinical trials that investigated the effect of QRS morphology on CRT, but only four trials [Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION), Cardiac Resynchronization - Heart Failure (CARE-HF), Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT), and Resynchronization-Defibrillation for Ambulatory Heart Failure Trial (RAFT)] included outcomes according to QRS morphology. They observed a 36% reduction in risk with the use of CRT [relative risk (RR) 0.64, 95% CI 0.52 to 0.77; p<0.00001] in left bundle branch block (LBBB) patients. However, the same benefit was not observed in patients with non-LBBB conduction abnormalities (RR 0.97, 95% CI 0.82 to 1.15; p<0.75)[8]. More than 10 PVCs per hour or runs of NSVT are acceptable markers of increased risk. If patients are symptomatic due to PVCs or NSVTs, or if PVCs or NSVTs contribute to reduced LVEF (tachycardia-induced cardiomyopathy), amiodarone or catheter ablation

Table 5. Recommended indications for CRT in patients with HF

Recommendations	COR	LOE
CRT is recommended in patients with an LVEF ≤35% and LBBB despite at least 3 months of guideline-directed medical therapy to reduce all-cause mortality who are expected to survive at least 1 year with good functional status:	I	
• With QRS duration >150 ms		A
• With QRS duration 130 to 150 ms		B
CRT should or may be considered in patients with LVEF ≤35% without LBBB despite at least 3 months of guideline-directed medical therapy to reduce all-cause mortality who are expected to survive at least 1 year with good functional status:		B
• With QRS duration >150 ms	IIa	
• With QRS duration 130 to 150 ms	IIb	
CRT should be considered in patients with chronic HF, QRS ≥120 ms, and LVEF ≤35% who remain in NYHA Functional Class III/ambulatory class IV despite at least 3 months of guideline-directed medical therapy to reduce all-cause mortality who are expected to survive at least 1 year with good functional status, provided that biventricular pacing as close as possible to 100% can be achieved.	IIa	A

COR=class of recommendation; CRT=cardiac resynchronization therapy; HF=heart failure; LBBB=left bundle branch block; LOE=level of evidence; LVEF=left ventricular ejection fraction; NYHA=New York Heart Association

Table 6. Recommended indications for CRT-D in patients with mild HF[10]

Recommendations	COR	LOE
CRT-D is recommended to reduce all-cause mortality in patients with QRS duration ≥130 ms, with LVEF ≤30%, and with LBBB despite at least 3 months of guideline-directed medical therapy who are expected to survive at least 1 year with good functional status.	I	A
CRT-D should be considered to prevent hospitalization for HF in patients with QRS duration ≥150 ms irrespective of QRS morphology and LVEF ≤35% despite at least 3 months of guideline-directed medical therapy who are expected to survive at least 1 year with good functional status.	IIa	A

COR=class of recommendation; CRT-D=cardiac resynchronization therapy with defibrillator; HF=heart failure; LBBB=left bundle branch block; LOE=level of evidence; LVEF=left ventricular ejection fraction

should be considered[9].

Summary of recommendations regarding optimal management of HF to reduce VAs

1. Guideline-directed medical therapy (ACEIs, beta-blockers, and MRA) is recommended to reduce the risk of sudden death and progressive HF.

2. Prompt identification and treatment of arrhythmogenic factors (e.g., pro-arrhythmic drugs, hypokalemia) and comorbidities (e.g., thyroid disease) is recommended.

3. ICD is recommended in patients with hemodynamically unstable VT/VF that are expected to survive for more than one year with good functional status.

4. Catheter ablation is recommended in patients with dilated cardiomyopathy (DCM) and bundle branch re-entry ventricular tachycardia that is refractory to medical therapy.

5. Amiodarone should be considered in patients with ICD who experience recurrent appropriate shocks despite optimal device programming.

6. Risk stratification of SCD by invasive electrophysiology study may be considered.

7. Amiodarone is not recommended for treatment of asymptomatic NSVT.

Conflicts of interest

The authors declare no conflict of interest.

References

1. Gupta S, Figueredo VM. Tachycardia mediated cardiomyopathy: pathophysiology, mechanisms, clinical features and management. Int J Cardiol 2014;172:40-6.
2. Chen J, Johnson G, Hellkamp AS, Anderson J, Mark DB, Lee KL, et al. Rapid-rate nonsustained ventricular tachycardia found on implantable cardioverter-defibrillator interrogation: relationship to outcomes in the SCD-HeFT (Sudden Cardiac Death in Heart Failure Trial). J Am Coll Cardiol 2013;61:2161-8.

3. Liao YC, Hsieh YC, Hung CY, Huang JL, Lin CH, Wang KY, et al. Statin therapy reduces the risk of ventricular arrhythmias, sudden cardiac death, and mortality in heart failure patients: a nationwide population-based cohort study. Int J Cardiol 2013;168:4805-7.
4. Sweeney MO. Sudden death in heart failure associated with reduced left ventricular function: substrates, mechanisms, and evidence-based management, Part II. Pacing Clin Electrophysiol 2001;24:1002-22.
5. Baldasseroni S, Opasich C, Gorini M, Lucci D, Marchionni N, Marini M, et al. Left bundle-branch block is associated with increased 1-year sudden and total mortality rate in 5517 outpatients with congestive heart failure: a report from the Italian network on congestive heart failure. Am Heart J 2002;143:398-405.
6. Packer DL, Prutkin JM, Hellkamp AS, Mitchell LB, Bernstein RC, Wood F, et al. Impact of implantable cardioverter-defibrillator, amiodarone, and placebo on the mode of death in stable patients with heart failure: analysis from the sudden cardiac death in heart failure trial. Circulation 2009;120:2170-6.
7. Connolly SJ, Hallstrom AP, Cappato R, Schron EB, Kuck KH, Zipes DP, et al. Meta-analysis of the implantable cardioverter defibrillator secondary prevention trials. AVID, CASH and CIDS studies. Antiarrhythmics vs implantable defibrillator study. cardiac arrest study Hamburg. Canadian implantable defibrillator study. Eur Heart J 2000;21:2071-8.
8. Sipahi I, Chou JC, Hyden M, Rowland DY, Simon DI, Fang JC. Effect of QRS morphology on clinical event reduction with cardiac resynchronization therapy: meta-analysis of randomized controlled trials. Am Heart J 2012;163:260-7.
9. Singh SN, Fisher SG, Carson PE, Fletcher RD. Prevalence and significance of nonsustained ventricular tachycardia in patients with premature ventricular contractions and heart failure treated with vasodilator therapy. Department of Veterans Affairs CHF STAT Investigators. J Am Coll Cardiol 1998;32:942-7.
10. Priori SG, Blomstrom-Lundqvist C, Mazzanti A, Blom N, Borggrefe M, Camm J, et al. 2015 ESC Guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: The task force for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death of the European Society of Cardiology (ESC). Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC). Eur Heart J 2015;36:2793-867.