

STATE-OF-THE-ART PAPERS

Nonsustained Ventricular Tachycardia

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Nonsustained ventricular tachycardia (NSVT) has been recorded in a wide range of conditions, from apparently healthy individuals to patients with significant heart disease. In the absence of heart disease, the prognostic significance of NSVT is debatable. When detected during exercise, and especially at recovery, NSVT indicates increased cardiovascular mortality within the next decades. In trained athletes, NSVT is considered benign when suppressed by exercise. In patients with non-ST-segment elevation acute coronary syndrome, NSVT occurring beyond 48 h after admission indicates an increased risk of cardiac and sudden death, especially when associated with myocardial ischemia. In acute myocardial infarction, in-hospital NSVT has an adverse prognostic significance when detected beyond the first 13 to 24 h. In patients with prior myocardial infarction treated with reperfusion and beta-blockers, NSVT is not an independent predictor of long-term mortality when other covariates such as left ventricular ejection fraction are taken into account. In patients with hypertrophic cardiomyopathy, and most probably genetic channelopathies, NSVT carries prognostic significance, whereas its independent prognostic ability in ischemic heart failure and dilated cardiomyopathy has not been established. The management of patients with NSVT is aimed at treating the underlying heart disease. (J Am Coll Cardiol 2012;60:1993-2004) © 2012 by the American College of Cardiology Foundation

Nonsustained ventricular tachycardia (NSVT) is defined as 3 (sometimes 5) or more consecutive beats arising below the atrioventricular node with an RR interval of <600 ms (>100 beats/min) and lasting <30 s (1). This definition, however, is not universal. NSVT has also been defined as runs of ≥ 16 beats with a rate ≥ 125 beats/min (2) or >120 beats/min (3), using a time cutoff of 15 s (4), or even without strictly defined diagnostic criteria (5). Thus, reliable epidemiological data on NSVT are difficult to obtain, particularly because reproducibility of NSVT recordings on Holter monitoring is documented in only half of the patients with this arrhythmia (6). Although NSVT may cause symptoms of palpitations, usually it is asymptomatic because of its brevity and the nature of the short-lived episodes of arrhythmia may not allow a clear distinction between monomorphic and polymorphic ventricular rhythms. When NSVT is documented in the context of a history of established monomorphic VT, it is usually monomorphic and may demonstrate the same morphology and

share the same mechanism with the clinical sustained arrhythmia, especially in cases of idiopathic VT.

In several clinical settings, NSVT is a marker of increased risk for subsequent sustained tachyarrhythmias and sudden cardiac death (SCD), whereas it may have no prognostic significance in others. The important tasks of the physician are to detect those apparently healthy individuals in whom NSVT represents a sign of occult disease, and to risk-stratify patients with known disease who present with this arrhythmia to provide therapy that mitigates associated risks. This may not always be easy in clinical practice. Whether NSVT provokes sustained, life-threatening arrhythmias or is simply a surrogate marker of a more severe underlying pathology is still unknown in most clinical settings.

NSVT in Apparently Normal Heart

In asymptomatic, apparently healthy persons, NSVT episodes may be recorded at rest (7-9). Although Framingham data have suggested an association with increased mortality (7), especially in persons with left ventricular hypertrophy (8), the prognostic significance of spontaneous NSVT recorded in apparently healthy individuals has not been established (9). Recent data have demonstrated that runs of ≥ 2 consecutive ventricular depolarizations during exercise or at recovery may occur in up to 3% of healthy men and predict an increase in cardiovascular mortality within the next 23 years by a factor of more than 2.5 (10). Frequent ventricular ectopy during recovery after exercise is a better

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Abbreviations and Acronyms

- ARVC** = arrhythmogenic right ventricular cardiomyopathy
- ECG** = electrocardiogram
- EPS** = electrophysiological study
- HCM** = hypertrophic cardiomyopathy
- ICD** = implantable cardioverter-defibrillator
- IHD** = ischemic heart disease
- LBBB** = left bundle branch block
- LQTS** = long QT syndrome
- LVEF** = left ventricular ejection fraction
- LVOT** = left ventricular outflow tract
- MI** = myocardial infarction
- MRI** = magnetic resonance imaging
- NSVT** = nonsustained ventricular tachycardia
- PVC** = premature ventricular contraction
- RBBB** = right bundle branch block
- RVOT** = right ventricular outflow tract
- SCD** = sudden cardiac death
- VF** = ventricular fibrillation

predictor of an increased risk of death than ventricular ectopy occurring only during exercise (11).

NSVT may also be recorded in professional athletes without structural heart disease but is considered benign and without long-term implications when suppressed by exercise (12–14). Arrhythmia episodes decrease during periods of deconditioning, and resumption of training is safe (15,16). The mechanism of NSVT in this setting is unknown. A shift of autonomic modulation from parasympathetic to sympathetic predominance induced by intensive endurance training and sinus bradycardia-induced ventricular ectopy have been postulated (15). NSVT in athletes is considered part of the “athlete’s heart syndrome” (12,15) and has no adverse prognostic significance, provided conditions such as hypertrophic cardiomyopathy (HCM), early repolarization syndrome, and other genetic channelopathies are excluded. The early repolarization pattern, manifested as QRS slurring or notching, has long been considered to be a benign electrocardiogram (ECG) manifestation that is seen more commonly in young healthy men and athletes (17), but there has been evidence suggesting that it may be associated with a risk for

ventricular fibrillation (VF), depending on the magnitude of the J wave and degree of ST elevation (18–22). A horizontal/descending type (defined as ≥ 0.1 mV elevation of the ST segment within 100 ms after the J point) may help to identify those individuals who are clearly at risk (23).

Age, general condition, previous medical history, history of sudden death and syncopal episodes in family members, and conditions such as electrolyte disturbances, metabolic imbalance, and proarrhythmic effect of drugs should be considered. Ischemic heart disease (IHD) should be excluded in patients age >40 years with episodes of NSVT. Before age 40 years, patients should be evaluated primarily to rule out nonischemic causes of arrhythmia, including latent hypertension and valve disease, cardiomyopathies, and inherited channelopathies such as long QT syndrome (LQTS), catecholaminergic polymorphic VT, Brugada syndrome, and other early repolarization syndromes that usually present with polymorphic episodes (Fig. 1, Table 1). Repetitive ectopics of the same morphology and monomorphic episodes, nonsustained or sustained, suggest idiopathic

VT or arrhythmogenic right ventricular cardiomyopathy (ARVC). Electrophysiology testing is usually performed as part of a planned ablation procedure in medically refractory patients and may be required to differentiate NSVT from short runs of atrial fibrillation in the context of an accessory pathway or other forms of aberration when this cannot be done from surface tracings (Table 1). When no pathology is identified, the tachycardia does not need specific therapy other than for symptomatic relief, but follow-up of the patient is advisable because inherited channelopathies may remain latent for several years (24).

Idiopathic VT. Monomorphic episodes of NSVT in apparently healthy individuals are often due to idiopathic ventricular outflow arrhythmias usually present in the form of repetitive uniform premature ventricular contractions (PVCs), repetitive monomorphic NSVT originally described by Gallavardin (that usually disappears as the heart rate increases with exercise), and paroxysmal sustained monomorphic VT (that is usually exercise provoked) (25,26). These tachycardias are adrenergically mediated and sensitive to adenosine or verapamil, which lower intracellular calcium level. Thus, triggered activity secondary to cAMP-mediated delayed after-depolarizations is the most probable mechanism (26). Tachycardias mainly (70% to 80%) arise in the right ventricular outflow tract (RVOT) and rarely below it, and 20% to 30% from the left ventricular outflow tract (LVOT). The tachycardia often occurs during exercise but disappears as the heart rate increases and returns during the recovery period (25). Repetitive behavior has also been documented in various clinical settings, including cardiomyopathy and previous myocardial infarction (MI) (27), as well as idiopathic VT originating in the aortic valve cusps (28). When

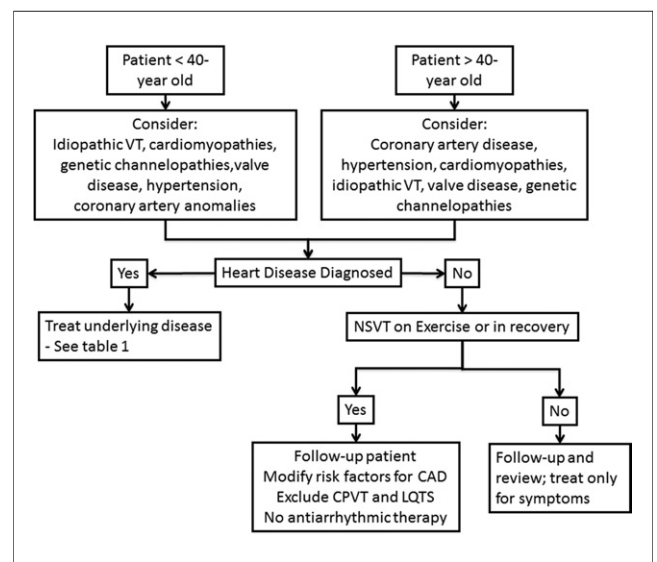


Figure 1 Clinical Approach to the Patient With NSVT

CAD = coronary artery disease; CPVT = catecholaminergic polymorphic ventricular tachycardia; LQTS = long QT syndrome; NSVT = nonsustained ventricular tachycardia; VT = ventricular tachycardia.

Table 1 Specific Management of NSVT

Clinical Setting	Investigations	Therapy
Idiopathic NSVT	Differentiate from ARVC	Beta-blockers, calcium-channel blockers; RF ablation if inducible sustained VT, progressively reduced LVEF, or symptoms
Arrhythmogenic ventricular cardiomyopathy	Value of EPS not established; NSVT indicates intermediate arrhythmic risk (<2% per year)	Not established; perhaps amiodarone or sotalolol; ICD frequently considered
Hypertension, valve disease	No need for specific management	Optimal antihypertensive therapy including beta-blockers
Non-STE ACS, NSVT >48 h after admission	Meticulous ischemia testing	Revascularization and optimal medical therapy*
Acute MI, NSVT >13–24 h until pre-discharge	Routine for acute MI	Revascularization and optimal medical therapy
Previous MI with LVEF of 31%–40%	Ischemia testing; EPS†	Revascularization and optimal medical therapy; if EP-inducible monomorphic VT or VF,‡ ICD§
Previous MI with LVEF ≤30% or LVEF ≤35% and NYHA functional class II/III	Ischemia testing; no EPS†	Revascularization and optimal medical therapy; ICD§
Asymptomatic CAD with EF >40%	Ischemia testing	Revascularization and optimal medical therapy; no need for specific NSVT therapy
Syncope in CAD with EF >40%	Ischemia testing; EP testing†	Revascularization and optimal medical therapy; if EP-inducible monomorphic VT or VF,‡ ICD
Nonischemic dilated cardiomyopathy	Value of EP testing not established	Optimal CCF therapy (medical and CRT if indicated); ablation for bundle branch re-entry; ICD for syncope or LVEF ≤35% and NYHA functional class II/III
Hypertrophic cardiomyopathy	Evaluate additional risk factors: previous cardiac arrest, unexplained syncope, massive LV hypertrophy (≥30 mm), hypotensive or attenuated blood pressure response to upright exercise	Beta-blockers; ICD, especially with frequent and prolonged (>10 beats) episodes of NSVT
Congenital heart disease (usually repaired Fallot)	EP testing	Predictive value of NSVT not established; consider corrective surgery; if VT inducible, ablation and ICD
Long QT syndrome	Genotype analysis useful	Beta-blockers; if syncope despite beta-blockers, ICD
Catecholaminergic polymorphic VT	Value of EP testing not established	Beta-blockers and perhaps calcium-channel blockers; if cardiac arrest, ICD
Brugada syndrome	Value of EP testing disputed	Possibly quinidine (more data needed); if cardiac arrest, ICD

*Optimal medical therapy for NSVT in the setting of CAD is defined as administration of beta-blockers (essential unless absolutely contraindicated), aspirin, statins, and angiotensin-converting enzyme inhibitors or angiotensin receptor blockers. †If conditions remain the same after indicated revascularization. ‡Prognostic significance of inducible monomorphic VT induced by 3 extrastimuli is similar to that of VT induced by 1 or 2 extrastimuli. Monomorphic VT, as opposed to VF, usually does not respond to revascularization. VF induced by 3 extrastimuli may represent a nonspecific response. §ICD is recommended if indications exist ≥40 days after MI.

ARVC = arrhythmogenic right ventricular cardiomyopathy; CAD = coronary artery disease; CCF = congestive cardiac failure; CRT = cardiac resynchronization therapy; EF = ejection fraction; EPS = electrophysiology study; ICD = implantable cardioverter-defibrillator; LVEF = left ventricular ejection fraction; MI = myocardial infarction; non-STE ACS = non-ST-segment elevation acute coronary syndrome (non-ST-segment elevation myocardial infarction or unstable angina); NSVT = nonsustained ventricular tachycardia; NYHA = New York Heart Association; RF = radiofrequency; VF = ventricular fibrillation; VT = ventricular tachycardia.

a 12-lead ECG displaying NSVT runs is available, RVOT tachycardias produce a left bundle branch block (LBBB) pattern with inferior axis and R/S transition at or beyond V₄. LVOT tachycardias may produce a right bundle branch block (RBBB) morphology with inferior axis and R/S transition at V₁ or V₂. The presence of NSVT in patients with idiopathic ventricular outflow tract arrhythmias indicates a higher propensity for inducibility of VT during intracardiac electrophysiology study (EPS) compared with isolated PVCs (48% vs. 4%). At exercise, the incidence of VT in this group is 10% (26). The diagnosis of RVOT idiopathic NSVT must be differentiated from that of ARVC or other forms of cardiomyopathy (Fig. 2) (29). This is not always straightforward because patients with RVOT VT may have subtle structural and functional abnormalities of the RVOT as detected by magnetic resonance imaging-(MRI) (30) or myocardial biopsy (31). QRS duration in lead I of >120 ms, earliest-onset QRS in lead V₁, QRS notching, and a transition of V₅ or later predict the presence

of ARVC (32). NSVT originating from the RVOT may occasionally cause syncope, although the risk of death is very low. Short cycle length during NSVT and history of syncope are predictors of coexistence of VF or polymorphic VT (33). In apparently normal hearts, NSVT due to bundle branch re-entry may be seen (34). The 12-lead ECG, when obtainable, may show either LBBB or RBBB pattern depending on the orientation of activation of the bundle branches. Microreentry within the Purkinje network may produce NSVT, or sustained VT, with a narrow QRS and RBBB with left axis (microreentry in the posterior fascicle), or rarely, inferior axis (anterior fascicle) (35,36).

In symptomatic patients, treatment should be directed toward relief of tachycardia-related symptoms with beta-blockers or calcium-channel blockers and adenosine, if needed in an acute setting. Class IC antiarrhythmic drugs, preferably in combination with beta-blockers (37), because, by definition, IHD or LV hypertrophy have been excluded, may also be tried. If medication is not effective, radiofre-

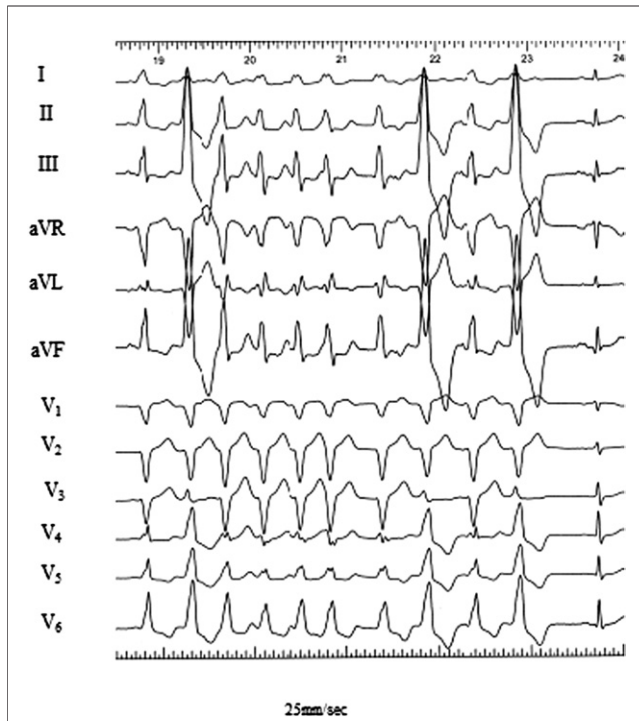


Figure 2 Runs of Pleomorphic (>1 Monomorphic Morphology) NSVT Recorded in a 52-Year-Old Man Referred for Catheter Ablation

Magnetic resonance imaging disclosed pathology of both the septal and lateral areas of the right ventricle, thus suggesting cardiomyopathy rather than idiopathic VT. The patient was treated with catheter ablation of the predominant ectopic morphology and cardioverter-defibrillator implantation. Abbreviations as in Figure 1.

quency catheter ablation is recommended and is successful in more than 80% of cases with a low risk of relapse during follow-up (38).

Genetic channelopathies. Patients with Brugada syndrome also have an apparently normal heart, and the resting ECG may not always display the typical Brugada type 1 pattern. Although there are no systematic studies evaluating prognostic significance of NSVT in Brugada syndrome, there is agreement that symptomatic patients (i.e., those with syncope or cardiac arrest) should be treated with implantable cardioverter-defibrillators (ICDs) (39).

Usually cardiac events in LQTS, which can also be latent, are due to prolonged NSVT episodes that might degenerate into VF (40). However, transient, asymptomatic runs of polymorphic NSVT are also common. The morphologically distinctive torsade de pointes QRS may also present as a nonsustained tachycardia that occurs in 3 common settings: congenital LQTS, drug-associated QT prolongation, and patients with advanced conduction system disease that has progressed to heart block (41). Typically, there is a long (600 to 800 ms) coupling interval of the initial beat of the torsades, whereas the last QRS complex of the episode is longer than the normal QRS during sinus rhythm. The tachycardia that usually occurs in the setting of bradycardia

or long post-ectopic pauses is often repetitive and may trigger VF. A variety of torsades initiating with a short coupling interval in patients without any evidence of LQTS and that could be nonsustained has also been described (42). Beta-blockers are the therapy of choice in patients with LQTS (43), but their effectiveness is reduced in LQT2 and LQT3 (44). Patients with recurrent syncope despite beta-blocker therapy as well as asymptomatic patients with a QTc >550 ms and additional risk factors should be considered for ICD therapy (45).

Exercise may also induce NSVT in patients with familial catecholaminergic polymorphic VT. Arrhythmias in this rare but very lethal condition may originate from the LVOT and less frequently from the RVOT or RV apex. QRS morphology suggests an outflow tract origin of the initiating beat in more than 50% of patients, and subsequent beats portray a polymorphic or typically bidirectional VT morphology (46). NSVT induced by treadmill exercise testing aimed at evaluating presumed LQTS suggests catecholaminergic polymorphic VT rather than LQTS (47). Beta-blocker therapy is the treatment of choice, probably together with calcium-channel blockers (48). Defibrillator implantation may be necessary in addition to beta-blockers in patients with syncope or VT (49).

Systemic Hypertension and Valve Disease

In systemic hypertension (50,51) and valvular disease (52), ventricular arrhythmias are common but less well characterized and usually represent polymorphic rhythms. In patients with arterial hypertension, NSVT is correlated with the degree of cardiac hypertrophy and subendocardial fibrosis. Approximately 12% to 28% of patients with hypertension and LV hypertrophy present with NSVT as opposed to 8% of patients with hypertension alone (50,51). The exact mechanism of ventricular arrhythmia in hypertension or valve disease is not known. Stretch-induced abnormal automaticity or triggered activity, fibrotic tissue and loss of connections between cell bundles that promotes re-entry, and subendocardial ischemia have been proposed (52).

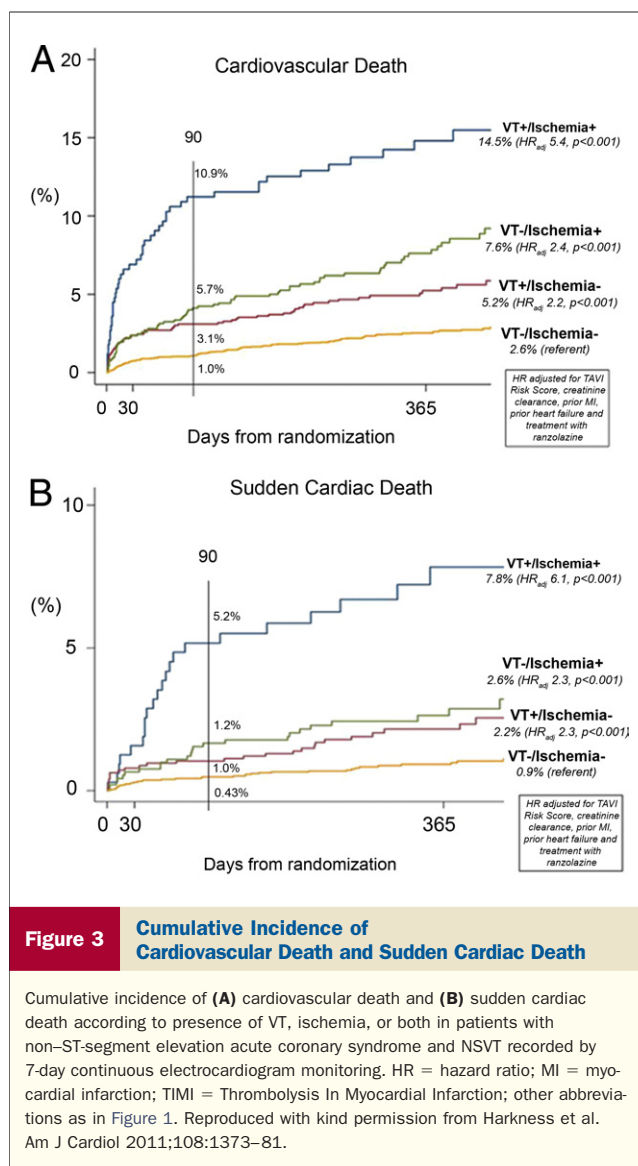
The prognostic value of NSVT in patients with lone hypertension (without evidence for concomitant IHD) remains unclear. In patients with valvular disease, the incidence of NSVT is considerable (up to 25% in aortic stenosis and in significant mitral regurgitation) and appears to be a marker of underlying LV pathology (52). Presence of NSVT is usually associated with LV hypertrophy or dysfunction, but no convincing evidence exists to prove that NSVT is an independent predictor of sudden death in patients with valve disease. Kilgfield et al. (53) estimated the annual risk of SCD in patients with mitral valve prolapse at 1.9 of 10,000 patients, lower than the annual risk of SCD from all causes in the adult population in the United States. A multivariate analysis also failed to identify ventricular arrhythmias (as opposed to New York Heart Association functional class, atrial fibrillation, and LV ejection fraction

[LVEF]) as an independent predictor of sudden death in mitral prolapse (54). Most of the reported patients with mitral valve prolapse demonstrate LBBB morphology during tachycardia, thus raising the possibility that the mitral valve prolapse might be an incidental finding or that the arrhythmia is due to other mechanisms not directly related to the mechanical stress imposed upon the ventricle by the valvular apparatus (54,55). The occurrence of NSVT in patients with hypertension requires evaluation of IHD. Aggressive treatment of hypertension (including beta-blockers) is the therapy of choice in patients with hypertension and NSVT. There is no evidence that NSVT after valve replacement carries adverse prognostic significance. The majority of patients with mitral valve prolapse and NSVT do not require extensive diagnostic evaluation or treatment (Table 1). In symptomatic patients with NSVT, beta-blockers are considered the first-line therapy.

Coronary Artery Disease

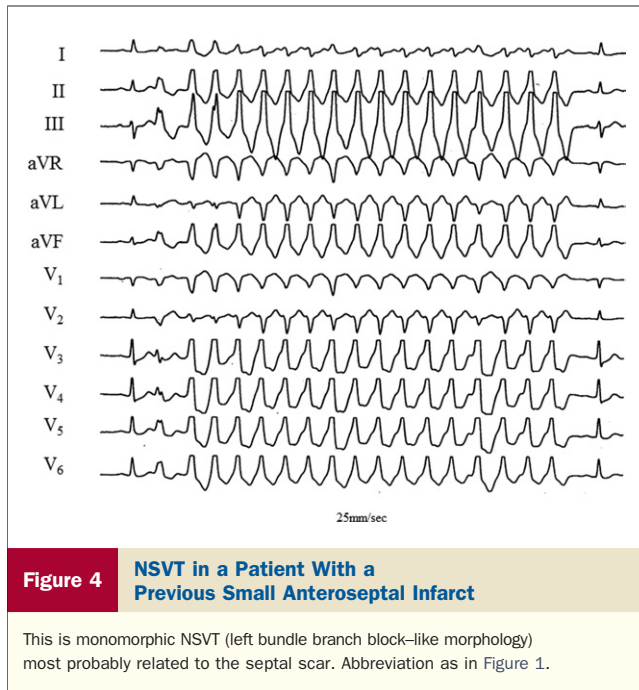
Non-ST-segment elevation acute coronary syndromes. In non-ST-segment elevation acute coronary syndromes, NSVT is detected in 18% to 25% of patients 2 to 9 days after admission (56), and even short episodes of VT lasting 4 to 7 beats are independently associated with the risk of SCD over the subsequent year. In the MERLIN-TIMI 36 (Metabolic Efficiency With Ranolazine for Less Ischemia in Non-ST-Elevation Acute Coronary Syndromes–Thrombolysis in Myocardial Infarction 36) trial in 6,300 patients who had 7-day continuous ECG monitoring, there was a >2-fold increase in the risk of SCD in patients with NSVT occurring >48 h after admission (56). There was no increased risk of SCD in patients with ventricular triplets, and earlier episodes within 48 h after admission did not carry the same risk. The coexistence of NSVT with myocardial ischemia, defined as >1 mm ST-segment depression lasting >1 min, indicated 10% risk of sudden death, with most episodes occurring within the first 3 months after the documentation of NSVT and ischemia (Fig. 3) (57).

Myocardial infarction. In acute MI, NSVT during the first 24 h is frequent (45% in patients without thrombolysis and up to 75% in reperfused patients) (1,58). Following the first 7 days after MI, NSVT is detected in approximately 6.8% to 13.4% of patients in the reperfusion era (59–62), which is not much different than that reported in the pre-thrombolysis era (63). The detected incidence of NSVT by a cardiac monitor implanted 2 to 5 days after MI in patients with LVEF ≤40% over a 2-year period was 13% (2). Usually monomorphic NSVT is seen in the context of re-entry at the borders of a ventricular scar due to previous MI, whereas ischemia most of the time induces polymorphic NSVT/VF (64). The QRS morphology during monomorphic tachycardia may show either RBBB or LBBB pattern or may even be nonspecific (Fig. 4). Both RBBB and LBBB patterns can be seen in the same patient when the infarct scar involves the interventricular



septum. The coexistence of necrotic and viable myocardium, as well as increased LV mass and end-systolic volume, predict NSVT (65).

In acute MI, NSVT during the first 13 (66) to 24 h (58) does not carry prognostic significance. In-hospital NSVT beyond this period indicates increased in-hospital mortality. Following discharge, NSVT after MI predicted higher long-term mortality in earlier studies (67,68). Evidence from the reperfusion era suggests that NSVT no longer appears to be an independent predictor of death in the patient with IHD if other factors such as EF are taken into account (4,59). NSVT has not been found to be an independent predictor of arrhythmic or total mortality in the studies of Hohnloser et al. (325 patients with MI) (60) and DANAMI-2 (Danish Trial in Acute Myocardial Infarction-2; 501 patients with fibrinolysis and 516 patients with primary angioplasty) (61). In a study of 2,130 infarct survivors, Makikallio et al. (69) reported that NSVT pre-



dicted SCD only in patients with LVEF >35%. No Holter variable was predictive of outcome in the presence of LVEF ≤35% (69). In the modern era, only the ATRAMI (Autonomic Tone and Reflexes After Myocardial Infarction) trial (1,071 post-MI patients) found NSVT to be an independent predictor of adverse prognosis (61). Recently, the CARISMA (Cardiac Arrhythmias and Risk Stratification After Acute Myocardial Infarction) Study Group (2) reported on long-term cardiac arrhythmias recorded by a cardiac monitor implanted 2 to 5 days after MI in 297 patients with LVEF ≤40%. NSVT (VT ≥125 beats/min for ≥16 beats lasting <30 s) was the most frequent ventricular arrhythmia recorded in the study (incidence of 13%) but was not associated with cardiac death over the next 2 years in multivariate analysis. With reperfusion and use of beta-blockers, therefore, NSVT after MI may not be an independent predictor of mortality, especially after EF is taken into account, and its prognostic significance is ambiguous.

Other clinical settings. The circumstances under which NSVT occurs are of clinical importance. MUSTT (Multi-center Unsustained Tachycardia Trial) data have shown a worse prognosis in patients with out-of-hospital, as opposed to in-hospital, identified NSVT (70). In patients subjected to surgical coronary revascularization, the occurrence of NSVT within the early (<10 days) post-revascularization period is associated with a far better outcome than when it occurs later after coronary artery bypass graft or in non-post-operative settings (71). However, when sustained VT is inducible in patients with early post-operative NSVT, the outcome is worse compared with that for noninducible patients (72). In the MUSTT study, racial differences were also shown to influence outcome of patients with NSVT

and reduced LV function (73). Few recent data on patients with stable IHD and LVEF >40% exist.

Clinical assessment of ischemic patients with NSVT. Tests of ischemia are mandatory. Acute myocardial ischemia is an established cause of polymorphic ventricular rhythms (64). The association of monomorphic NSVT, a substrate-dependent arrhythmia, with acute ischemia is less well characterized, but ischemia may induce sustained or nonsustained monomorphic VT in the presence of a myocardial scar (74,75).

Echocardiography may detect signs of cardiomyopathy or other structural abnormalities and impaired LV function. There has been overwhelming evidence that in patients with heart disease in general, LVEF is the major determinant of cardiac and total mortality (3,4,76). However, LVEF does not always predict ICD intervention in patients with ischemic or nonischemic cardiomyopathy (77), and analysis of arrhythmic death in 674 patients enrolled in the MUSTT study showed that patients whose only risk factor was EF ≤30% had a predicted 2-year arrhythmic death risk ≤5% (78).

Holter monitoring is a valuable diagnostic tool for detecting patients with NSVT, and 7-day Holter monitoring improves the detection of ventricular arrhythmic episodes (79). However, the suppression of frequent ventricular ectopy or NSVT runs with antiarrhythmic drugs does not imply a favorable diagnosis (80) and may increase mortality (81,82). Thus, Holter monitoring may be useful for risk stratification purposes by means of detecting episodes of NSVT in certain clinical settings, but its use for the subsequent follow-up and evaluation of treatment is limited.

The major utility of EPS testing in patients with NSVT and IHD is for LVEF between 30% and 40%. In NSVT in the context of reduced LVEF (<40%), inducibility of sustained monomorphic VT at baseline EPS was associated with a 2-year actuarial risk of sudden death or cardiac arrest of 50% compared with a 6% risk in patients without inducible VT (83). Noninducible patients in the MUSTT study had a significantly lower risk of cardiac arrest or sudden death compared with inducible patients at 2 and 5 years (12% vs. 24% and 18% vs. 32%, respectively) (84), and the higher percentage of events that were arrhythmic among patients with inducible tachyarrhythmia appeared more distinct among patients with an EF ≥30% (61% of events were arrhythmic among inducible and only 42% among noninducible patients, $p = 0.002$) (85).

The results of the ATRAMI trial (61) regarding the prognostic significance of heart rate variability have not been reproduced by other studies (86–88), and autonomic markers, as well as signal-averaged ECG, in the beta-blocking era have limited predictive power in identifying patients at risk of SCD (89). Promising results on the predictive ability of T-wave alternans tests have not been consistent (90–92). In patients with LVEF <40% and NSVT, strategies employing microvolt T-wave alternans,

EPS, or both might identify subsets of patients least likely to benefit from ICD insertion (93).

Therapy of ischemic patients with NSVT. The treatment of ischemic patients with NSVT should first include modern therapy for IHD, such as revascularization, beta-blockers, statins, and angiotensin II receptor blockers or angiotensin-converting enzyme inhibitors. Revascularization and beta-blockade seem to be especially important in acute coronary syndromes in this respect (57). Flecainide (81,82) and sotalol (94) increase mortality, whereas amiodarone shows a trend toward reducing arrhythmia episodes but without significantly affecting total mortality (95,96) or even showing a trend toward increasing it (97). Therefore, no antiarrhythmic drug is suitable for primary prevention of cardiac death with exception for beta-blockers, which were shown in several studies to reduce total and cardiac mortality in post-infarction patients, at least during the first year post-MI (98). There are no data indicating that NSVT in post-infarction patients with EF >40% requires specific antiarrhythmic therapy apart from beta-blockade. The role of EPS-guided therapy in these patient populations remains to be determined. Patients presenting with syncope and with inducible VF, or especially monomorphic VT, should be considered for ICD in the absence of reversible ischemia (Table 1).

LV Dysfunction and Heart Failure

In patients with ischemic and nonischemic heart failure and LVEF <30% to 40%, the reported prevalence of NSVT is 30% to 80% (99,100). In dilated cardiomyopathy, NSVT has been detected in 40% to 50% of patients (101–103). In approximately 10% of the cases of idiopathic dilated cardiomyopathy, sustained or nonsustained VT is due to bundle branch re-entry (104). These tachycardias are usually unstable, and the 12-lead ECG may show either LBBB or RBBB pattern.

No convincing data on the predictive ability of NSVT exist in patients with heart failure. The GESICA-GEMA (Grupo de Estudio de la Sobrevida en la Insuficiencia Cardíaca en Argentina–Grupo de Estudios Multicéntricos en Argentina) investigators identified NSVT as an independent predictor of total mortality in 516 patients with heart failure (35% to 40% IHD) and LVEF \leq 35% (99); NSVT detected on Holter monitoring and lack of use of beta-blockers, but not LVEF, have been found predictive for ICD-derived arrhythmias in patients with ischemic or nonischemic cardiomyopathy (77). However, after adjustment for other variables and especially for LVEF, NSVT was not an independent predictor of sudden death or total mortality in 674 patients with heart failure and LVEF <35% to 50% (70% to 75% IHD) who were enrolled in the CHF STAT (Survival Trial of Antiarrhythmic Therapy in Congestive Heart Failure) (80,100). Similar results were published by the PROMISE (Prospective Randomized Milrinone Survival Evaluation) investigators; 1,080 patients

with New York Heart Association class III/IV symptoms and LVEF \leq 35% were enrolled in the PROMISE study (5). Only during the recovery period after exercise has frequent ventricular ectopy been found to carry an adverse prognostic significance in patients with heart failure (105). There is also no consistency in reports investigating the association between NSVT and cardiac mortality in series with nonischemic dilated cardiomyopathy only. In the Marburg cardiomyopathy study, arrhythmia risk stratification was performed on 343 patients with dilated cardiomyopathy (3). On multivariate analysis, only LVEF was found to be a significant predictor of major arrhythmic events, with a relative risk of 2.3 per 10% decrease of EF. However, patients with NSVT in the context of LVEF <30% had an 8-fold arrhythmia risk compared with patients with LVEF >30% without NSVT (3). Recently, LVEF, NSVT, and steeper QT_e slope (assessed by dedicated software) were found to be significant predictors of arrhythmic events (106). Interestingly, after medical stabilization with angiotensin-converting enzyme inhibitors and beta-blockers, the number and length of NSVT runs did not increase the risk of major ventricular arrhythmias in patients with LVEF \leq 35% as opposed to those with LVEF >35% (107).

Clinical assessment and therapy. The most useful risk stratifier is still LVEF despite its limitations, and recommendations for ICD are mainly based on LVEF and symptomatic status of heart failure. In ischemic patients, programmed stimulation is indicated in the presence of NSVT when LVEF is 30% to 40%, as previously discussed. The prognostic usefulness of programmed stimulation in patients with nonischemic dilated cardiomyopathy, including those with NSVT, remains controversial (108,109). There has been some evidence that inducibility of ventricular arrhythmias (110) and especially polymorphic VT or VF (111) indicates increased likelihood of subsequent ICD therapies and might be considered a useful risk stratifier. In patients with nonischemic cardiomyopathy, signal-averaged ECG does not predict sudden death (3), and results on the value of heart rate variability have also been conflicting (112,113).

Amiodarone therapy was associated with decreased mortality in the GESICA trial (97), whereas no such effect was observed in the CHF-STAT trial (80) or the SCD-HeFT (Sudden Cardiac Death in Heart Failure Trial) (114). Dronedarone also did not fulfill hopes regarding its prevention of mortality in patients with heart failure (115). Certain patients with NSVT in the context of reduced LV function need an ICD, as has been demonstrated in the MADIT (Multicenter Automatic Defibrillator Implantation Trial) (116), MUSTT (117), MADIT II (118), and SCD-HeFT (114) trials (Table 1). ICDs, however, should be considered \geq 40 days after MI to achieve reduction of total mortality (119,120).

Although according to the SCD-HeFT study, patients with symptomatic heart failure and LVEF \leq 35% are treated with ICD with or without additional cardiac resynchroni-

zation therapy, the value of ICD for primary prevention in nonischemic dilated cardiomyopathy with (121,122) or without (123) NSVT is debatable. No single trial has demonstrated a reduction in total (as opposed to arrhythmic) mortality in this setting.

Hypertrophic Cardiomyopathy

There is no characteristic ECG morphology of NSVT in patients with HCM. Up to 20% to 30% of patients may have NSVT, whereas this proportion approaches 80% in patients with a history of cardiac arrest (124–126). Relatively slow, often asymptomatic NSVT episodes may be documented on prolonged ambulatory recordings. When nonsustained or sustained VT is induced by programmed stimulation, it is more often polymorphic than monomorphic (126). However, these estimations may not reflect the true incidence of NSVT in HCM because they are based on highly selected referral populations. In patients with HCM, the presence of delayed enhancement on contrast-enhanced MRI (127) or of echocardiographic 2-dimensional strain, which is used to identify myocardial fibrosis, in more than 3 LV segments (128) is associated with increased likelihood of NSVT. Frequent and prolonged (>10 beats) episodes of nonsustained VT on Holter monitoring most probably indicate an increased risk of sudden death in HCM, especially in young patients (125). Recent MRI studies support this notion. NSVT was reported in 31% of 178 patients with HCM; for sudden death, NSVT had negative and positive predictive values of 95% and 9% and sensitivity and specificity of 45% and 69%, respectively (129). In another report, NSVT, but not myocardial fibrosis, was an independent predictor of arrhythmic events and death (130).

Beta-blockers may decrease the risk of sudden death, but defibrillator implantation is the therapy of choice in the presence of high-risk factors, including frequent NSVT accompanied by history of syncope or family history of sudden death at young age, may justify defibrillator implantation as primary prevention in patients with HCM (131).

Arrhythmogenic Right Ventricular Cardiomyopathy

The tachycardias in ARVC arise from the right ventricle and typically present with LBBB morphology with a left or even right axis deviation (132).

Patients with ARVC may present with asymptomatic NSVT despite only subtle RV abnormalities and have a trend for an increased arrhythmic risk and a rate of appropriate ICD intervention of 3.7% per year (133). The results of antiarrhythmic medications are disappointing, and ICD seems to be the therapy of choice in patients with cardiac arrest, syncope, or hemodynamically poorly tolerated VT despite antiarrhythmic therapy. Catheter ablation of VT when feasible is successful in reducing further episodes but cannot offer absolute protection without ICD backup (134).

Other Conditions

Giant-cell myocarditis is a cause of monomorphic or polymorphic VT that is usually sustained and associated with high mortality (135). Ventricular extrasystolic activity can be detected with Holter monitoring in up to 50% of patients with repaired tetralogy of Fallot, and recent studies have detected a 4% to 14% prevalence of sustained VT (136–138). Inducible sustained monomorphic or polymorphic VT is an independent risk factor for subsequent events in patients with repaired tetralogy of Fallot (137). Complex ventricular arrhythmias are common in AL amyloidosis (57% of patients have PVCs and 18% NSVT) and carry prognostic significance (139). Cardiac sarcoidosis may present with nonsustained polymorphic or monomorphic VT that usually responds to steroids. Development of sustained monomorphic VT is an ominous sign, and ICD may be indicated (140). Patients with Chagas cardiomyopathy presenting with either sustained VT or NSVT have a major risk for mortality in the presence of moderate LV systolic dysfunction (LVEF <40%) (141). In patients with tachycardiopathy, the presence of NSVT, in addition to the PVC burden, longer PVC duration, multiform PVCs, and RV PVCs, may be associated with the development of cardiomyopathy (142). Eradication of the arrhythmia may result in restoration of LV function.

Conclusions

NSVT can be recorded in a wide range of conditions, in apparently healthy individuals to patients with significant heart disease. Its prognostic significance varies, depending on the underlying condition, and in several clinical settings is not known. The management of patients with NSVT is aimed at treating the underlying heart disease rather than the arrhythmia itself, unless serious symptoms occur.

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REFERENCES

1. Katritsis DG, Camm AJ. Nonsustained ventricular tachycardia: where do we stand? *Eur Heart J* 2004;25:1093–9.
2. Bloch Thomsen PE, Jons C, Raatikainen MJ, et al. Long-term recording of cardiac arrhythmias with an implantable cardiac monitor in patients with reduced ejection fraction after acute myocardial infarction: the Cardiac Arrhythmias and Risk Stratification After Acute Myocardial Infarction (CARISMA) study. *Circulation* 2010; 122:1258–64.
3. Grimm W, Christ M, Bach J, Müller HH, Maisch B. Noninvasive arrhythmia risk stratification in idiopathic dilated cardiomyopathy: results of the Marburg cardiomyopathy study. *Circulation* 2003;108: 2883–91.
4. Caruso AC, Marcus FI, Hahn EA, Hartz VL, Mason JW. Predictors of arrhythmic death and cardiac arrest in the ESVEM trial. *Electrophysiologic Study Versus Electromagnetic Monitoring*. *Circulation* 1997;96:1888–92.
5. Teerlink JR, Jalaluddin M, Anderson S, et al. Ambulatory ventricular arrhythmias in patients with heart failure do not specifically predict

- an increased risk of sudden death. PROMISE (Prospective Randomized Milrinone Survival Evaluation) Investigators. *Circulation* 2000;101:40–6.
- Senges JC, Becker R, Schreiner KD, et al. Variability of Holter electrocardiographic findings in patients fulfilling the noninvasive MADIT criteria. Multicenter Automatic Defibrillator Implantation Trial. *Pacing Clin Electrophysiol* 2002;25:183–90.
 - Bikkina M, Larson MG, Levy D. Prognostic implications of asymptomatic ventricular arrhythmias: the Framingham heart study. *Ann Int Med* 1992;117:990–6.
 - Bikkina M, Larson MG, Levy D. Asymptomatic ventricular arrhythmias and mortality risk in subjects with left ventricular hypertrophy. *J Am Coll Cardiol* 1993;22:1111–6.
 - Engstrom G, Hedblad B, Janzon L, et al. Ventricular arrhythmias during 24-h ambulatory ECG recording: incidence, risk factors and prognosis in men with and without a history of cardiovascular disease. *J Intern Med* 1999;246:363–72.
 - Jouven X, Zureik M, Desnos M, Courbon D, Ducimetiere P. Long-term outcome in asymptomatic men with exercise-induced premature ventricular depolarizations. *N Engl J Med* 2000;343:826–33.
 - Frolkis JP, Pothier CE, Blackstone EH, Lauer MS. Frequent ventricular ectopy after exercise as a predictor of death. *N Engl J Med*. 2003;348:781–90.
 - Biffi A, Pelliccia A, Verdile L, et al. Long-term clinical significance of frequent and complex ventricular tachyarrhythmias in trained athletes. *J Am Coll Cardiol* 2002;40:446–52.
 - Baltesberger S, Bauersfeld U, Candinas R, et al. Sinus node disease and arrhythmias in the long-term follow-up of former professional cyclists. *Eur Heart J* 2008;29:71–8.
 - Biffi A, Maron BJ, Di Giacinto B, et al. Relation between training-induced left ventricular hypertrophy and risk for ventricular tachyarrhythmias in elite athletes. *Am J Cardiol* 2008;101:1792–5.
 - Biffi A, Maron BJ, Verdile L, et al. Impact of physical deconditioning on ventricular tachyarrhythmias in trained athletes. *J Am Coll Cardiol* 2004;44:1053–8.
 - Biffi A, Maron BJ, Culasso F, et al. Patterns of ventricular tachyarrhythmias associated with training, deconditioning and retraining in elite athletes without cardiovascular abnormalities. *Am J Cardiol* 2011;107:697–703.
 - Surawicz B, Macfarlane PW. Inappropriate and confusing electrocardiographic terms J-wave syndromes and early repolarization. *J Am Coll Cardiol* 2011;57:1584–6.
 - Antzelevitch C, Yan GX. J wave syndromes. *Heart Rhythm* 2010;7:549–58.
 - Tikkanen JT, Anttonen O, Junttila MJ, et al. Long-term outcome associated with early repolarization on electrocardiography. *N Engl J Med* 2009;361:2529–37.
 - Haissaguerre M, Derval N, Sacher F, et al. Sudden cardiac arrest associated with early repolarization. *N Engl J Med* 2008;358:2016–23.
 - Watanabe H, Makiyama T, Koyama T, et al. High prevalence of early repolarization in short QT syndrome. *Heart Rhythm* 2010;7:647–52.
 - Cappato R, Furlanello F, Giovannozzo V, et al. J wave, QRS slurring, and ST elevation in athletes with cardiac arrest in the absence of heart disease: marker of risk or innocent bystander? *Circ Arrhythm Electrophysiol* 2010;3:305–11.
 - Tikkanen JT, Junttila MJ, Anttonen O, et al. Early repolarization: electrocardiographic phenotypes associated with favorable long-term outcome. *Circulation* 2011;123:2666–73.
 - Lehnart SE, Ackerman MJ, Benson DW Jr., et al. Inherited arrhythmias: a National Heart, Lung, and Blood Institute and Office of Rare Diseases workshop consensus report about the diagnosis, phenotyping, molecular mechanisms, and therapeutic approaches for primary cardiomyopathies of gene mutations affecting ion channel function. *Circulation* 2007;116:2325–45.
 - Katritsis D, Gill J, Camm AJ. Repetitive monomorphic ventricular tachycardia. In: Zipes DP, Jalife J, editors. *Clinical Electrophysiology: From Cell to Bedside*. 2nd edition. Philadelphia, PA: Saunders, 1995:900–6.
 - Kim RJ, Iwai S, Markowitz SM, Shah BK, Stein KM, Lerman BB. Clinical and electrophysiological spectrum of idiopathic ventricular outflow tract arrhythmias. *J Am Coll Cardiol* 2007;49:2035–43.
 - Buxton AE, Marschinski FE, Doherty JU, et al. Repetitive monomorphic ventricular tachycardia: clinical and electrophysiologic characteristics in patients with and patients without organic heart disease. *Am J Cardiol* 1984;54:997–1002.
 - Ouyang F, Fotuhi P, Ho SY, et al. Repetitive monomorphic ventricular tachycardia originating from the aortic sinus cusp: electrocardiographic characterization for guiding catheter ablation. *J Am Coll Cardiol* 2002;39:500–8.
 - Marcus FI, McKenna WJ, Sherrill D, et al. Diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: proposed modification of the Task Force Criteria. *Eur Heart J* 2010;31:806–14.
 - Carlson MD, White RD, Trohman RG, et al. Right ventricular outflow tract ventricular tachycardia: detection of previously unrecognized anatomic abnormalities using cine magnetic resonance imaging. *J Am Coll Cardiol* 1994;24:720–7.
 - Chimenti C, Calabrese F, Thiene G, Pieroni M, Maseri A, Frustaci A. Inflammatory left ventricular microaneurysms as a cause of apparently idiopathic ventricular tachyarrhythmias. *Circulation* 2001;104:168–73.
 - Hoffmayer KS, Machado ON, Marcus GM, et al. Electrocardiographic comparison of ventricular arrhythmias in patients with arrhythmogenic right ventricular cardiomyopathy and right ventricular outflow tract tachycardia. *J Am Coll Cardiol* 2011;58:831–8.
 - Shimizu W. Arrhythmias originating from the right ventricular outflow tract: how to distinguish “malignant” from “benign”? *Heart Rhythm* 2009;6:1507–11.
 - Blanck Z, Jazayeri M, Dhala A, Deshpande S, Sra J, Akhtar M. Bundle branch reentry: a mechanism of ventricular tachycardia in the absence of myocardial or valvular dysfunction. *J Am Coll Cardiol* 1993;22:1718–22.
 - Katritsis D, Ahsan A, Anderson M, et al. Catheter ablation for successful management of fascicular tachycardia. An approach guided by the recording of fascicular potentials. *Heart* 1996;75:384–8.
 - Ouyang F, Cappato R, Ernst S, et al. Electroanatomic substrate of idiopathic left ventricular tachycardia: unidirectional block and macroreentry within the Purkinje network. *Circulation* 2002;105:462–9.
 - Myerburg RJ, Kessler KM, Cox MM, et al. Reversal of proarrhythmic effects of flecainide acetate and encainide hydrochloride by propranolol. *Circulation* 1989;80:1571–9.
 - Stevenson WG, Soejima K. Catheter ablation for ventricular tachycardia. *Circulation* 2007;115:2750–60.
 - Antzelevitch C, Brugada P, Borggrefe M, et al. Brugada syndrome: report of the second consensus conference: endorsed by the Heart Rhythm Society and the European Heart Rhythm Association. *Circulation* 2005;111:659–70.
 - Zareba W, Moss AJ, le Cessie S, et al. Risk of cardiac events in long QT syndrome family members. *J Am Coll Cardiol* 1995;26:1685–91.
 - Morita H, Wu J, Zipes DP. The QT syndromes: long and short. *Lancet* 2008;372:750–63.
 - Leenhardt A, Glaser E, Burguera M, Nurnberg M, Maison-Blanche P, Coumel P. Short-coupled variant of torsade de pointes: a new electrocardiographic entity in the spectrum of idiopathic ventricular tachyarrhythmias. *Circulation* 1993;89:206–15.
 - Goldenberg I, Bradley J, Moss A, et al. Beta-blocker efficacy in high-risk patients with the congenital long-QT syndrome types 1 and 2: implications for patient management. *J Cardiovasc Electrophysiol* 2010;21:893–901.
 - Priori SG, Napolitano C, Schwartz PJ, et al. Association of long QT syndrome loci and cardiac events among patients treated with beta-blockers. *JAMA* 2004;292:1341–4.
 - Schwartz PJ, Spazzolini C, Priori SG, et al. Who are the long-QT syndrome patients who receive an implantable cardioverter-defibrillator and what happens to them?: data from the European Long-QT Syndrome Implantable Cardioverter-Defibrillator (LQTS ICD) registry. *Circulation* 2010;122:1272–82.
 - Sy RW, Gollob MH, Klein GJ, et al. Arrhythmia characterization and long-term outcomes in catecholaminergic polymorphic ventricular tachycardia. *Heart Rhythm* 2011;8:864–71.
 - Horner JM, Ackerman MJ. Ventricular ectopy during treadmill exercise stress testing in the evaluation of long QT syndrome. *Heart Rhythm* 2008;5:1690–4.
 - Rosso R, Kalman JM, Rogowski O, et al. Calcium channel blockers and beta-blockers versus beta-blockers alone for preventing exercise-

- induced arrhythmias in catecholaminergic polymorphic ventricular tachycardia. *Heart Rhythm* 2007;4:1149–54.
49. European Heart Rhythm Association, Heart Rhythm Society, Zipes DP, et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death). *J Am Coll Cardiol* 2006;48:e247–346.
 50. McLenaghan JM, Henderson E, Morris KI, Dargie HJ. Ventricular arrhythmias in patients with hypertensive left ventricular hypertrophy. *N Engl J Med* 1987;317:787–92.
 51. Pringle SD, Dunn FG, Macfarlane PW, McKillop JH, Lorimer AR, Cobbe SM. Significance of ventricular arrhythmias in systemic hypertension with left ventricular hypertrophy. *Am J Cardiol* 1992;69:913–7.
 52. Martínez-Rubio A, Schwammenthal Y, Schwammenthal E, et al. Patients with valvular heart disease presenting with sustained ventricular tachyarrhythmias and syncope. Results of programmed ventricular stimulation and long-term follow-up. *Circulation* 1997;96:500–8.
 53. Kilgfield P, Levy D, Devreux RB, Savage DD. Arrhythmias and sudden death in mitral valve prolapse. *Am Heart J* 1987;113:1298–307.
 54. Grigioni F, Enriquez-Sarano M, Ling LH, et al. Sudden death in mitral regurgitation due to flail leaflet. *J Am Coll Cardiol* 1999;34:2078–85.
 55. Avierinos JF, Gersh BJ, Melton LJ III, et al. Natural history of asymptomatic mitral valve prolapse in the community. *Circulation* 2002;106:1355–61.
 56. Scirica BM, Braunwald E, Belardinelli L, et al. Relationship between nonsustained ventricular tachycardia after non-ST-elevation acute coronary syndrome and sudden cardiac death: observations from the Metabolic Efficiency With Ranolazine for Less Ischemia in Non-ST-Elevation Acute Coronary Syndrome-Thrombolysis in Myocardial Infarction 36 (MERLIN-TIMI 36) randomized controlled trial. *Circulation* 2010;122:455–62.
 57. Harkness JR, Morrow DA, Braunwald E, et al. Myocardial ischemia and ventricular tachycardia on continuous electrocardiographic monitoring and risk of cardiovascular outcomes after non-ST-segment elevation acute coronary syndrome (from the MERLIN-TIMI 36 trial). *Am J Cardiol* 2011;108:1373–81.
 58. Heidbüchel H, Tack J, Vanneste L, Ballet A, Ector H, Van de Werf F. Significance of arrhythmias during the first 24 hours of acute myocardial infarction treated with alteplase and effect of early administration of a beta-blocker or a bradycardiac agent on their incidence. *Circulation* 1994;89:1051–9.
 59. Maggioni AP, Zuanetti G, Franzosi MG, et al. Prevalence and prognostic significance of ventricular arrhythmias after acute myocardial infarction in the fibrinolytic era: GISSI-2 results. *Circulation* 1993;87:312–22.
 60. Hohnloser SH, Klingenhoben T, Zabel M, et al. Prevalence, characteristics and prognostic value during long-term follow-up of non-sustained ventricular tachycardia after myocardial infarction in the thrombolytic era. *J Am Coll Cardiol* 1999;33:1895–902.
 61. La Rovere MT, Pinna GD, Hohnloser SH, et al. Autonomic tone and reflexes after myocardial infarction. Baroreflex sensitivity and heart rate variability in the identification of patients at risk for life-threatening arrhythmias: implications for clinical trials. *Circulation* 2001;103:2072–7.
 62. Höfsten DE, Wachtell K, Lund B, Mølgaard H, Egstrup K. Prevalence and prognostic implications of non-sustained ventricular tachycardia in ST-segment elevation myocardial infarction after revascularization with either fibrinolysis or primary angioplasty. *Eur Heart J* 2007;28:407–14.
 63. Bigger JT Jr., Fleiss JL, Rolnitzky LM. Prevalence, characteristics and significance of ventricular tachycardia detected by 24-hour continuous electrocardiographic recordings in the late hospital phase of acute myocardial infarction. *Am J Cardiol* 1986;58:1151–60.
 64. Wolfe CL, Nibley C, Bhandari A, Chatterjee K, Scheinman M. Polymorphous ventricular tachycardia associated with acute myocardial infarction. *Circulation* 1991;84:1543–51.
 65. Di Bella G, Passino C, Aquaro GD, et al. Different substrates of non-sustained ventricular tachycardia in post-infarction patients with and without left ventricular dilatation. *J Card Fail* 2010;16:61–8.
 66. Cheema AN, Sheu K, Parker M, Kadish AH, Goldberger JJ. Nonsustained ventricular tachycardia in the setting of acute myocardial infarction: tachycardia characteristics and their prognostic implications. *Circulation* 1998;98:2030–6.
 67. Multicenter Post-Infarction Research Group. Risk stratification and survival after myocardial infarction. *N Engl J Med* 1983;309:331–6.
 68. Mukharji J, Rude RE, Poole WK, et al. Risk factors for sudden death after acute myocardial infarction: two-year follow-up. *Am J Cardiol* 1984;54:31–6.
 69. Makikallio TH, Barthel P, Schneider R, et al. Prediction of sudden cardiac death after acute myocardial infarction: role of Holter monitoring in the modern treatment era. *Eur Heart J* 2005;26:762–9.
 70. Pires LA, Lehmann MH, Buxton AE, Hafley GE, Lee KL. The Multicenter Unsustained Tachycardia Trial Investigators. Differences in inducibility and prognosis of in-hospital versus out-of-hospital identified nonsustained ventricular tachycardia in patients with coronary artery disease: clinical and trial design implications. *J Am Coll Cardiol* 2001;38:1156–62.
 71. Pires LA, Hafley GE, Lee KL, et al. Prognostic significance of nonsustained ventricular tachycardia after coronary bypass surgery in patients with left ventricular dysfunction. *J Cardiovasc Electrophysiol* 2002;13:757–63.
 72. Mittal S, Lomnitz DJ, Mirchandani S, et al. Prognostic significance of nonsustained ventricular tachycardia after revascularization. *J Cardiovasc Electrophysiol* 2002;13:342–6.
 73. Russo AM, Hafley GE, Lee KL, et al. Racial differences in outcome in the Multicenter Unsustained Tachycardia Trial (MUSTT): a comparison of whites versus blacks. *Circulation* 2003;108:67–72.
 74. Furukawa T, Moroe K, Mayrovitz HN, Sampell R, Myerburg RJ. Arrhythmogenic effects of graded coronary blood flow reduction superimposed upon prior myocardial infarction in dogs. *Circulation* 1991;84:368–77.
 75. Garan H, McComb JM, Ruskin JN. Spontaneous and electrically induced ventricular arrhythmias during acute ischemia superimposed on 2 week old canine myocardial infarction. *J Am Coll Cardiol* 1988;11:603–11.
 76. Camm AJ, Katritsis D. Risk stratification of patients with ventricular arrhythmias. In: Zipes DP, Jalife J, editors: *Clinical Electrophysiology: From Cell to Bedside*. 3rd edition. Philadelphia, PA: Saunders, 2000:808–27.
 77. Verma A, Sarak B, Kaplan AJ, et al. Predictors of appropriate implantable cardioverter defibrillator (ICD) therapy in primary prevention patients with ischemic and nonischemic cardiomyopathy. *Pacing Clin Electrophysiol* 2010;33:320–9.
 78. Buxton AE, Lee KL, Hafley GE, et al. Limitations of ejection fraction for prediction of sudden death risk in patients with coronary artery disease: lessons from the MUSTT study. *J Am Coll Cardiol* 2007;50:1150–7.
 79. Pastor-Pérez FJ, Manzano-Fernández S, Goya-Esteban R, et al. Comparison of detection of arrhythmias in patients with chronic heart failure secondary to non-ischemic versus ischemic cardiomyopathy by 1 versus 7-day Holter monitoring. *Am J Cardiol* 2010;106:677–81.
 80. Singh SN, Fletcher RD, Fisher SG, et al. Amiodarone in patients with congestive heart failure and asymptomatic ventricular arrhythmia. Survival Trial of Antiarrhythmic Therapy in Congestive Heart Failure. *N Engl J Med* 1995;333:77–82.
 81. Cardiac Arrhythmia Suppression Trial (CAST) Investigators. Preliminary report: effect of encainide and flecainide on mortality in a randomized trial of arrhythmia suppression after myocardial infarction. *N Engl J Med* 1989;321:406–12.
 82. Cardiac Arrhythmia Suppression Trial-II Investigators. Effect of antiarrhythmic agent moricizine on survival after myocardial infarction. The Cardiac Arrhythmia Suppression Trial-II. *N Engl J Med* 1992;327:227–33.
 83. Wilber DJ, Olshansky B, Moran JF, Scanlon PJ. Electrophysiological testing and nonsustained ventricular tachycardia. Use and limitations in patients with coronary artery disease and impaired ventricular function. *Circulation* 1990;82:350–8.
 84. Buxton AE, Lee KL, DiCarlo L, et al. Electrophysiologic testing to identify patients with coronary artery disease who are at risk for sudden

- death. Multicenter Unsustained Tachycardia Trial Investigators. *N Engl J Med* 2000;342:1937–45.
85. Buxton AE, Lee KL, Hafley GE, et al. Relation of ejection fraction and inducible ventricular tachycardia to mode of death in patients with coronary artery disease: an analysis of patients enrolled in the Multicenter Unsustained Tachycardia Trial. *Circulation* 2002;106:2466–72.
86. Huikuri HV, Tapanainen JM, Lindgren K, et al. Prediction of sudden cardiac death after myocardial infarction in the beta-blocking era. *J Am Coll Cardiol* 2003;42:652–8.
87. Abildstrom SZ, Jensen BT, Agner E, et al. Heart rate versus heart rate variability in risk prediction after myocardial infarction. *J Cardiovasc Electrophysiol* 2003;14:168–73.
88. Bauer A, Guzik P, Barthel P, et al. Reduced prognostic power of ventricular late potentials in post-infarction patients of the reperfusion era. *Eur Heart J* 2005;26:755–61.
89. Stein KM. Noninvasive risk stratification for sudden death: signal-averaged electrocardiography, nonsustained ventricular tachycardia, heart rate variability, baroreflex sensitivity, and QRS duration. *Prog Cardiovasc Dis* 2008;51:106–17.
90. Bloomfield DM, Steinman RC, Namerow PB, et al. Microvolt T-wave alternans distinguishes between patients likely and patients not likely to benefit from implanted cardiac defibrillator therapy: a solution to the Multicenter Automatic Defibrillator Implantation Trial (MADIT) II conundrum. *Circulation* 2004;110:1885–9.
91. Amit G, Rosenbaum DS, Super DM, Costantini O. Microvolt T-wave alternans and electrophysiologic testing predict distinct arrhythmia substrates: implications for identifying patients at risk for sudden cardiac death. *Heart Rhythm* 2010;7:763–8.
92. Chow T, Kereiakes DJ, Onufer J, et al. Does microvolt T-wave alternans testing predict ventricular tachyarrhythmias in patients with ischemic cardiomyopathy and prophylactic defibrillators? The MASTER (Microvolt T Wave Alternans Testing for Risk Stratification of Post-Myocardial Infarction Patients) trial. *J Am Coll Cardiol* 2008;52:1607–15.
93. Costantini O, Hohnloser SH, Kirk MM, et al. The ABCD (Alternans Before Cardioverter Defibrillator) trial: strategies using T-wave alternans to improve efficiency of sudden cardiac death prevention. *J Am Coll Cardiol* 2009;53:471–9.
94. Waldo AL, Camm AJ, deRuiter H, et al. Effect of d-sotalol on mortality in patients with left ventricular dysfunction after recent and remote myocardial infarction. The SWORD Investigators. *Survival With Oral d-Sotalol*. *Lancet* 1996;348:7–12.
95. Cairns JA, Connolly SJ, Gent M, et al. Post-myocardial infarction mortality in patients with ventricular premature depolarizations. *Circulation* 1991;84:550–7.
96. Julian DG, Camm AJ, Frangin J, et al. Randomised trial of effect of amiodarone on mortality in patients with left ventricular dysfunction after recent myocardial infarction: EMIAT. *Lancet* 1997;349:662–3.
97. Elizari MV, Martínez JM, Belziti C, et al. Morbidity and mortality following early administration of amiodarone in acute myocardial infarction. GEMICA Study Investigators, GEMA Group, Buenos Aires, Argentina. Grupo de Estudios Multicéntricos en Argentina. *Eur Heart J* 2000;21:198–205.
98. Viscoli CM, Horwitz RI, Singer BH. Beta-blockers after myocardial infarction: influence of first-year clinical course on long-term effectiveness. *Ann Intern Med* 1993;118:99–105.
99. Doval HC, Nul DR, Grancelli HO, et al. Nonsustained ventricular tachycardia in severe heart failure. Independent marker of increased mortality due to sudden death. GESICA-GEMA Investigators. *Circulation* 1996;94:3198–203.
100. 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. *J Am Coll Cardiol* 1998;32:942–7.
101. Meinertz T, Hofmann T, Kasper W, et al. Significance of ventricular arrhythmias in idiopathic dilated cardiomyopathy. *Am J Cardiol* 1984;53:902–7.
102. Neri R, Mestroni L, Salvi A, Camerini F. Arrhythmias in dilated cardiomyopathy. *Postgrad Med J* 1986;62:593–7.
103. Olshausen KV, Stienen U, Schwartz F, et al. Long-term prognostic significance of ventricular arrhythmias in idiopathic dilated cardiomyopathy. *Am J Cardiol* 1988;61:146–51.
104. Soejima K, Stevenson WG, Sapp JL, Selwyn AP, Couper G, Epstein LM. Endocardial and epicardial radiofrequency ablation of ventricular tachycardia associated with dilated cardiomyopathy: the importance of low-voltage scars. *J Am Coll Cardiol* 2004;43:1834–42.
105. O'Neill JO, Young JB, Pothier CE, et al. Severe frequent ventricular ectopy after exercise as a predictor of death in patients with heart failure. *J Am Coll Cardiol* 2004;44:820–6.
106. Iacoviello M, Forleo C, Guida P, et al. Ventricular repolarization dynamicity provides independent prognostic information toward major arrhythmic events in patients with idiopathic dilated cardiomyopathy. *J Am Coll Cardiol* 2007;50:225–31.
107. Zecchin M, Di Lenarda A, Gregori D, et al. Are nonsustained ventricular tachycardias predictive of major arrhythmias in patients with dilated cardiomyopathy on optimal medical treatment? *Pacing Clin Electrophysiol* 2008;31:290–9.
108. Grimm W, Hoffmann J, Menz V, et al. Programmed ventricular stimulation for arrhythmia risk prediction in patients with idiopathic dilated cardiomyopathy and nonsustained ventricular tachycardia. *J Am Coll Cardiol* 1998;32:739–45.
109. Brilakis ES, Shen WK, Hammill SC, et al. Role of programmed ventricular stimulation and implantable cardioverter defibrillators in patients with idiopathic dilated cardiomyopathy and syncope. *Pacing Clin Electrophysiol* 2001;24:1623–30.
110. Daubert JP, Winters SL, Subacius H, et al. Ventricular arrhythmia inducibility predicts subsequent ICD activation in nonischemic cardiomyopathy patients: a DEFINITE substudy. *Pacing Clin Electrophysiol* 2009;32:755–61.
111. Rolf S, Haverkamp W, Borggreve M, Breithardt G, Bocker D. Induction of ventricular fibrillation rather than ventricular tachycardia predicts tachyarrhythmia recurrences in patients with idiopathic dilated cardiomyopathy and implantable cardioverter defibrillator for secondary prophylaxis. *Europace* 2009;11:289–96.
112. Fauchier L, Babuty D, Cosnay P, et al. Prognostic value of heart rate variability for sudden death and major arrhythmic events in patients with idiopathic dilated cardiomyopathy. *J Am Coll Cardiol* 1999;33:1203–7.
113. Rashba EJ, Estes NA, Wang P, et al. Preserved heart rate variability identifies low-risk patients with nonischemic dilated cardiomyopathy: results from the DEFINITE trial. *Heart Rhythm* 2006;3:281–6.
114. Bardy GH, Lee KL, Mark DB, et al. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. *N Engl J Med* 2005;352:225–37.
115. Kober L, Torp-Pedersen C, McMurray JVV, et al. Increased mortality after dronedarone therapy for severe heart failure. *N Engl J Med* 2008;358:2678–87.
116. Moss AJ, Hall WJ, Cannom DS, et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. Multicenter Automatic Defibrillator Implantation Trial Investigators. *N Engl J Med* 1996;335:1933–40.
117. Buxton AE, Lee KL, Fisher JD, et al. A randomized study of the prevention of sudden death in patients with coronary artery disease. Multicenter Unsustained Tachycardia Trial Investigators. *N Engl J Med* 1999;341:1882–90.
118. Goldenberg I, Gillespie J, Moss AJ, et al. Long-term benefit of primary prevention with an implantable cardioverter-defibrillator: an extended 8-year follow-up study of the Multicenter Automatic Defibrillator Implantation Trial II. *Circulation* 2010;122:1265–71.
119. Hohnloser SH, Kuck KH, Dorian P, et al. Prophylactic use of an implantable cardioverter-defibrillator after acute myocardial infarction. *N Engl J Med* 2004;351:2481–8.
120. Steinbeck G, Andresen D, Seidl K, et al. Defibrillator implantation early after myocardial infarction. *N Engl J Med* 2009;361:1427–36.
121. Kadish A, Dyer A, Daubert JP, et al. Prophylactic defibrillator implantation in patients with nonischemic dilated cardiomyopathy. *N Engl J Med* 2004;350:2151–7.
122. Strickberger SA, Hummel JD, Bartlett TG, et al. Amiodarone versus implantable cardioverter-defibrillator: randomized trial in patients with nonischemic dilated cardiomyopathy and asymptomatic nonsustained ventricular tachycardia—AMIOVIRT. *J Am Coll Cardiol* 2003;41:1707–12.
123. Bänsch D, Antz M, Boczor S, et al. Primary prevention of sudden cardiac death in idiopathic dilated cardiomyopathy: the Cardio-myopathy Trial (CAT). *Circulation* 2002;105:1453–8.

124. Spirito P, Rapezzi C, Autore C, et al. Prognosis of asymptomatic patients with hypertrophic cardiomyopathy and nonsustained ventricular tachycardia. *Circulation* 1994;90:2743–7.
125. Monserrat L, Elliott PM, Gimeno JR, Sharma S, Penas-Lado M, McKenna WJ. Non-sustained ventricular tachycardia in hypertrophic cardiomyopathy: an independent marker of sudden death risk in young patients. *J Am Coll Cardiol* 2003;42:873–9.
126. Fananapazir L, Epstein SE. Hemodynamic and electrophysiologic evaluation of patients with hypertrophic cardiomyopathy surviving cardiac arrest. *Am J Cardiol* 1991;67:280–7.
127. Adabag AS, Maron BJ, Appelbaum E, et al. Occurrence and frequency of arrhythmias in hypertrophic cardiomyopathy in relation to delayed enhancement on cardiovascular magnetic resonance. *J Am Coll Cardiol* 2008;51:1369–74.
128. Di Salvo G, Pacileo G, Limongelli G, et al. Non sustained ventricular tachycardia in hypertrophic cardiomyopathy and new ultrasonic derived parameters. *J Am Soc Echocardiogr* 2010;23:581–90.
129. Adabag AS, Casey SA, Kuskowski MA, Zenovich AG, Maron BJ. Spectrum and prognostic significance of arrhythmias on ambulatory Holter electrocardiogram in hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2005;45:697–704.
130. O'Hanlon R, Grasso A, Roughton M, et al. Prognostic significance of myocardial fibrosis in hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2010;56:867–74.
131. Maron BJ. Contemporary insights and strategies for risk stratification and prevention of sudden death in hypertrophic cardiomyopathy. *Circulation* 2010;121:445–56.
132. Basso C, Corrado D, Marcus FI, et al. Arrhythmogenic right ventricular cardiomyopathy. *Lancet* 2009;373:1289–300.
133. Corrado D, Calkins H, Link MS, et al. Prophylactic implantable defibrillator in patients with arrhythmogenic right ventricular cardiomyopathy/dysplasia and no prior ventricular fibrillation or sustained ventricular tachycardia. *Circulation* 2010;122:1144–52.
134. Arbelo E, Josephson ME. Ablation of ventricular arrhythmias in arrhythmogenic right ventricular dysplasia. *J Cardiovasc Electrophysiol* 2010;21:473–86.
135. Cooper LT Jr, Berry GJ, Shabetai R. Idiopathic giant-cell myocarditis—natural history and treatment. Multicenter Giant Cell Myocarditis Study Group Investigators. *N Engl J Med* 1997;336:1860–6.
136. Gatzoulis MA, Balaji S, Webber SA, et al. Risk factors for arrhythmia and sudden cardiac death late after repair of tetralogy of Fallot: a multicentre study. *Lancet* 2000;356:975–81.
137. Khairy P, Landzberg MJ, Gatzoulis MA, et al. Value of programmed ventricular stimulation after tetralogy of Fallot repair: a multicenter study. *Circulation* 2004;109:1994–2000.
138. Khairy P, Aboulhosn J, Gurvitz MZ, et al. Arrhythmia burden in adults with surgically repaired tetralogy of Fallot: a multi-institutional study. *Circulation* 2010;122:868–75.
139. Palladini G, Malamani G, Cò F, et al. Holter monitoring in AL amyloidosis: prognostic implications. *Pacing Clin Electrophysiol* 2001;24:1228–33.
140. Winters SL, Cohen M, Greenberg S, et al. Sustained ventricular tachycardia associated with sarcoidosis: assessment of the underlying cardiac anatomy and the prospective utility of programmed ventricular stimulation, drug therapy and an implantable antitachycardia device. *J Am Coll Cardiol* 1991;18:937–43.
141. Sarabanda AV, Marin-Neto JA. Predictors of mortality in patients with Chagas' cardiomyopathy and ventricular tachycardia not treated with implantable cardioverter-defibrillators. *Pacing Clin Electrophysiol* 2011;34:54–62.
142. Munoz FD, Syed FF, Noheria A, et al. Characteristics of premature ventricular complexes as correlates of reduced left ventricular systolic function: study of the burden, duration, coupling interval, morphology and site of origin of PVCs. *J Cardiovasc Electrophysiol* 2011;22:791–8.

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