PVCS & SUDDEN CARDIAC DEATH

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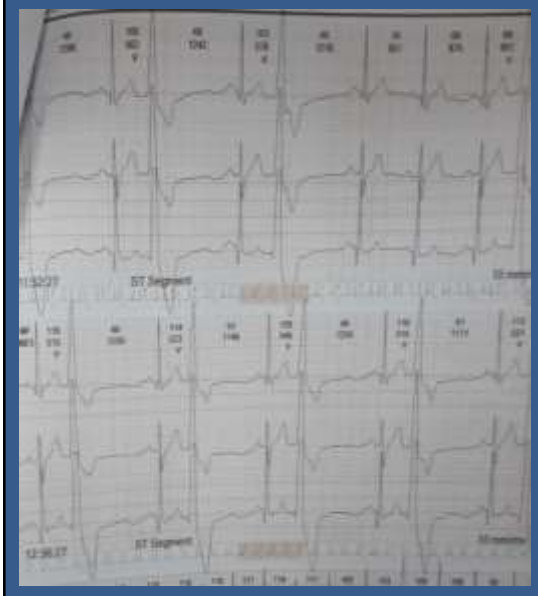
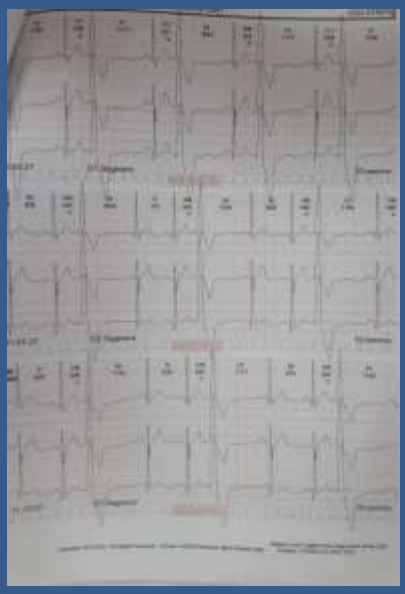
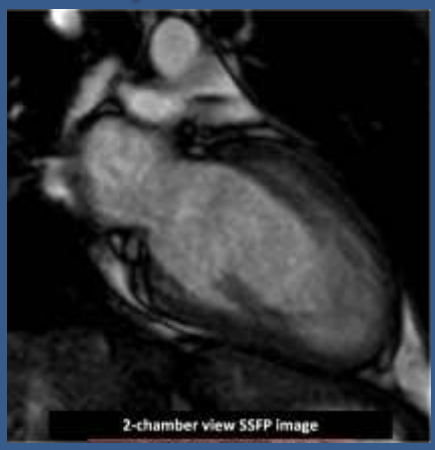




Cardiovascular Magnetic Resonance Report

2- Structure –

Spongy non-compacted myocardium is seen at apex, apical anterior, apical lateral, and the mid anterolatel segments. Definitive criteria for LV non-compaction are fulfilled. **(Definitive criteria : non-compacted to compacted myocardium ratio at end-diastole >2.3).**



Definition

- PVCs are early depolarizations originating in the ventricle due to increased automaticity.
- NSVT occurs when three or more consecutive PVCs occur at a rate greater than 100 beats-per-minute. They may be monomorphic or polymorphic and are often present in patients presenting with nonspecific cardiac symptoms.

PVCs are common with an estimated prevalence of 1% to 4% in the general population on standard 12-lead electrocardiography and between 40% and 75% of subjects on 24- to 48-hour Holter monitoring

Their prevalence is generally age-dependent, ranging from 1% in children 11 years old to 69% in subjects 75 years

While PVCs and NSVT are frequently seen in the general population and are sometimes considered clinically insignificant, they mark a population at increased risk for cardiac disease including SCD and cardiomyopathy.

Traditionally, they have been thought to be relatively benign in the absence of structural heart disease but they represent increased risk of sudden death in structural heart disease

Pathophysiology

There are three major concerns regarding the presence of PVCs and NSVT.

a. The substrate often associated with PVCs & NSVT increases the risk for sustained VT.

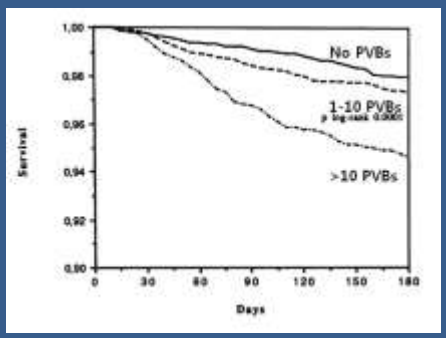
b. Another concern, particularly with increased automaticity and polymorphic VT, is that a PVC may be coupled closely with the preceding QRS complex and produce ventricular fibrillation.

c. In addition, frequent ventricular ectopy is known to adversely affect cardiac function itself, namely tachycardia-induced cardiomyopathy.

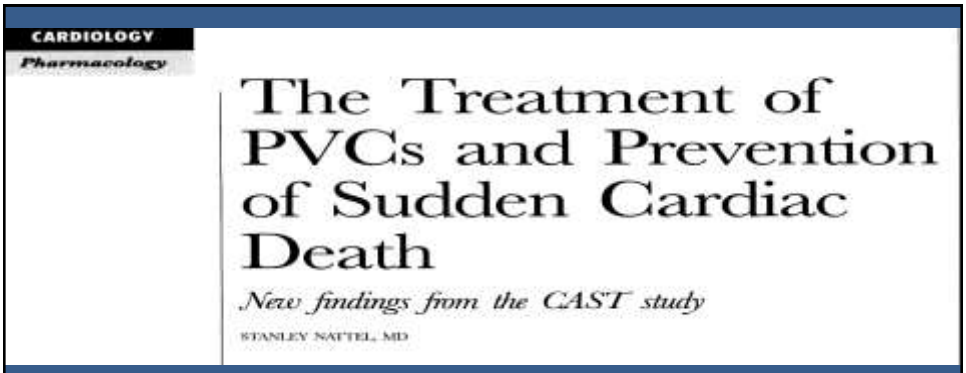
PVCs in structural heart disease

- The incidence, frequency, and complexity of ventricular arrhythmias were greater in the presence of known or suspected heart disease.
- PVCs and runs of NSVT in subjects with structural heart disease contribute to an increased mortality risk, the magnitude of which varies with the nature and extent of the underlying disease.

Coronary Artery Disease



6-month survival of patients by premature ventricular contractions (PVCs) per hour *Adapted from Maggioni et al*



- The trial was intended to run for several years, but was stopped prematurely because the mortality rate was more than doubled by the two drugs Flecainide and encainide.
- Most deaths were sudden and occurred despite over 90% suppression ofventricular ectopy.

Heart Failure

- The prevalence and complexity of ambulatory ventricular arrhythmias increase dramatically as LV function deteriorates.
- In patients with a LVEF of less than 40%, the prevalence of NSVT rises from 15-20% in patients with class I-II symptoms of heart failure to 40-55% in class II-III patients and 50-70% in class III-IV patients

Ambulatory Ventricular Arrhythmias in Patients With Heart Failure Do Not Specifically Predict an Increased Risk of Sudden Death

John R. Teerlink, MD; Muhammad Jalaluddin, MS; Susan Anderson, MS; Marrick L. Kukin, MD; Eric J. Eichhorn, MD; Gary Francis, MD; Milton Packer, MD; Barry M. Massie, MD; on Behalf of the PROMISE (Prospective Randomized Milrinone Survival Evaluation) Investigators*

- The Prospective Randomized Milrinone Survival Evaluation (PROMISE) study was undertaken to determine whether ventricular arrhythmias were independent and specific predictors of sudden death. In this study, ventricular arrhythmias did not specifically define a group at high risk for sudden death and did not provide significant incremental prognostic information beyond readily available clinical variables .

The presence of complex PVCs & NSVT on ambulatory monitoring predicts total cardiac mortality but does not identify patients who are destined to die suddenly

- This observation suggests that the frequency and complexity of rhythm disturbances in patients with severe heart failure reflect the severity of the underlying disease process rather than a specific arrhythmogenic state.

- NSVT should not guide therapeutic interventions, such as the institution of antiarrhythmic therapy or implantation of antifibrillatory device

PVCs in structurally normal hearts

- PVCs and NSVT that are observed in patients without overt structural heart disease are considered idiopathic .
- Idiopathic VA usually originates from the outflow tract region , generally considered benign, although in some cases they can lead to severe symptoms and/or cardiomyopathy
- It is important to rule out conditions which may be associated with malignant VA originating from the outflow tract, such as ARVC, Brugada syndrome or catecholaminergic polymorphic VT.
- After excluding these potential malignant causes of VA, some patients with idiopathic VA are at risk of SCD (although this risk is rare).

The "Short-Coupled" Variant of Right Ventricular Outflow Ventricular Tachycardia: A Not-So-Benign Form of Benign Ventricular Tachycardia?

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Right Ventricular Outflow Ventricular Tachycardia. Idiopathic ventricular tachycardia (VT) originating from the right ventricular outflow tract (RVOT-VT) and idiopathic RVOT-extrasystoles are generally considered benign arrhythmias. We described three cases who originally presented with typical "benign looking" RVOT-extrasystoles or RVOT-VT but developed malignant polymorphic VT during follow-up. The unusual aspect of their RVOT-extrasystoles was their coupling interval, which appears to be intermediate between the ultra-short coupling interval of idiopathic VF and the long coupling interval seen in the truly benign RVOT-VT. *(J Cardiovasc Electrophysiol, Vol. 16, pp. 912-916, August 2005)*

In the study of Viskin *et al., the coupling intervals of the initiating PVC in those with* idiopathic VF, malignant RVOT VT, and benign RVOT VT was 300 ± 40 ms, 340 ± 30 ms, and 427 ± 76 ms, respectively

Mapping and Ablation of Idiopathic Ventricular Fibrillation

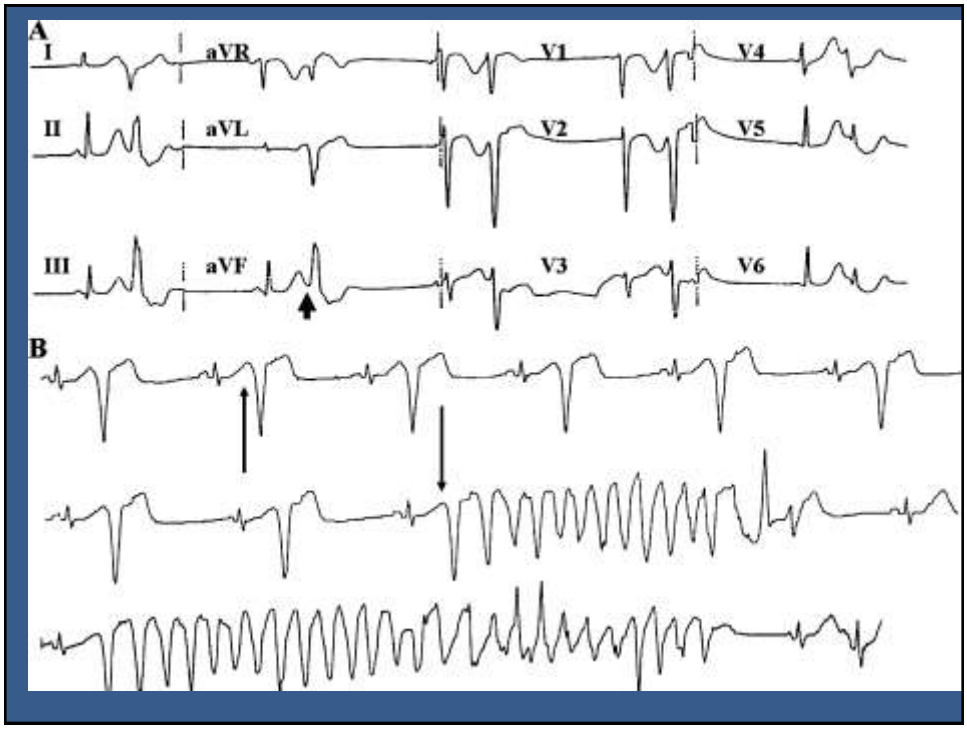
Michel Haïssaguerre, MD; Morio Shoda, MD; Pierre Jaïs, MD; Akihiko Nogami, MD; Dipen C. Shah, MD; Josef Kautzner, MD; Thomas Arentz, MD; Dietrich Kalushe, MD; Dominique Lamaison, MD; Mike Griffith, MD; Fernando Cruz, MD; Angelo de Paola, MD; Fiorenzo Gaïta, MD; Mélèze Hocini, MD; Stéphane Garrigue, MD; Laurent Macle, MD; Rukshen Weerasooriya, MD; Jacques Clémenty, MD

Background—Ventricular fibrillation is the main mechanism of sudden cardiac death. The feasibility of eliminating recurrent episodes by catheter ablation has not been reported.

Methods and Results—Twenty-seven patients without known heart disease (13 men, 14 women, 41±14 years of age) were studied after being resuscitated from recurrent (10±12) episodes of primary idiopathic ventricular fibrillation; 23 had received a defibrillator. The first initiating beat of ventricular fibrillation had an identical electrocardiographic morphology and coupling interval (297±41 ms) to preceding isolated premature beats typically noted in the aftermath of resuscitation. These triggers were localized by mapping the earliest electrical activity and ablated by local radiofrequency delivery. Outcome was assessed by Holter and defibrillator memory interrogation. Premature beats were elicited from the Purkinje conducting system in 23 patients: from the left ventricular septum in 10, from the anterior right ventricle in 9, and from both in 4. The interval from the Purkinje potential to the following myocardial activation varied from 10 to 150 ms during premature beat but was 11±5 ms during sinus rhythm, indicating location at peripheral Purkinje arborization. The premature beats originated from the right ventricular outflow tract muscle in 4 patients. The accuracy of mapping was confirmed by acute elimination of premature beats during local radiofrequency delivery. During a follow-up of 24±28 months, 24 patients (89%) had no recurrence of ventricular fibrillation without drug.

Conclusions—Primary idiopathic ventricular fibrillation is a syndrome characterized by dominant triggers from the distal Purkinje system. These sources can be eliminated by focal energy delivery. (*Circulation*. 2002;106:962-967.)

- The available data suggest that the shorter CI of initiating PVCs correlates with the more malignant form of RVOT VT but that a cutoff value that would reliably differentiate malignant RVOT VT from benign RVOT VT remains to be defined.
- Moreover, long CI does not necessarily guarantee absence of risk.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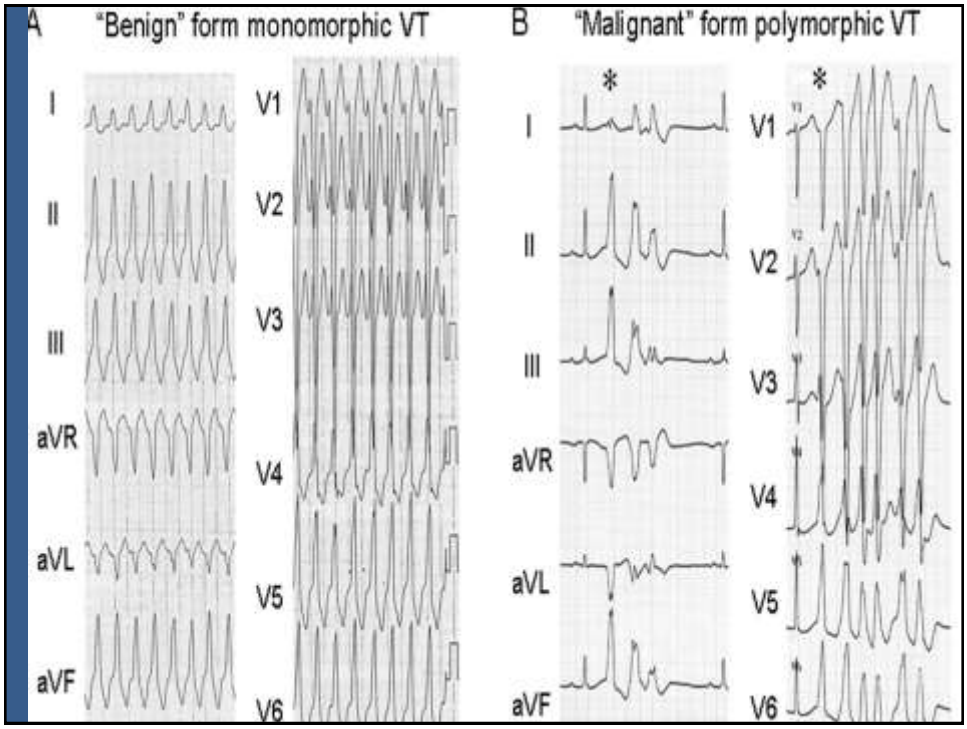
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"Benign" form monomorphic VT
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"Malignant" form polymorphic VT
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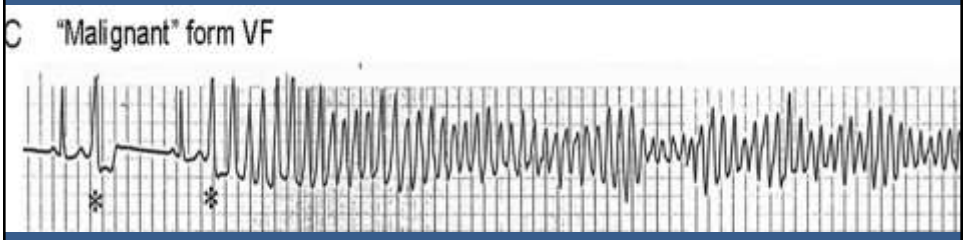


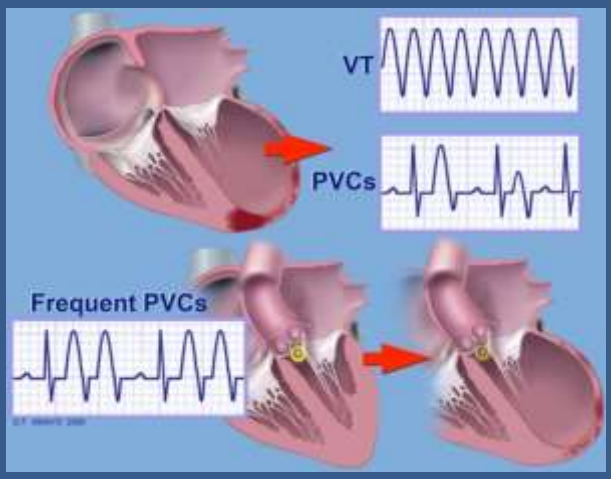
- Igarashi *et al. suggested that a prematurity index (the* coupling interval divided by the QT interval of the preceding sinus complex) <0.73 can identify malignant PVCs with a sensitivity of 91% and a specificity of 44%

Recognizing Malignant Idiopathic PVCs & NSVA

- Pre-syncope or syncope as the first symptom
- Shorter cycle length of NSVT on Holter recordings
- the coupling interval of PVCs triggering malignant VT or VF is shorter than PVC's triggering benign VT
- PVCs with ultra-short coupling interval ("R-on-T" extrasystoles falling on the peak of the Twave) are an ominous sign in patients with idiopathic VF.

Relationship to Cardiomyopathy

Primary arrhythmia or primary cardiomyopathy



First Evidence of Premature Ventricular Complex-Induced Cardiomyopathy: A Potentially Reversible Cause of Heart Failure

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From the Cardiovascular Division, Department of Internal Medicine, Mayo Clinic and Mayo Foundation, Rochester, Minnesota

PVC-Induced Cardiomyopathy. Tachycardia-induced cardiomyopathy is a well-recognized and reversible condition, but left ventricular dysfunction due to frequent isolated premature ventricular complexes (PVCs) has not been reported. We observed resolution of dilated cardiomyopathy in a patient after a focal source of PVCs was eliminated by radiofrequency ablation. In a subset of patients with heart failure, PVC-induced cardiomyopathy may be a potentially reversible cause of left ventricular dysfunction. *(J Cardiovasc Electrophysiol, Vol. 11, pp. 328-329, March 2000)*

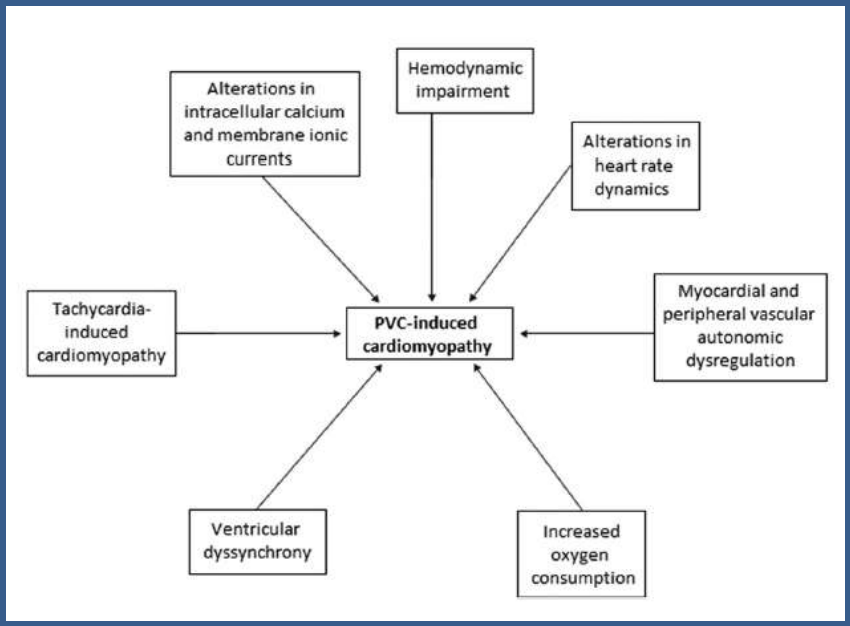
Characteristics of primary cardiomyopathy versus tachycardia-induced cardiomyopathy

	PVCs resulting from cardiomyopathy	PVCs causing cardiomyopathy
Patient Characteristics	**Older patients with known cardiovascular disease**	**Otherwise healthy individuals**
Comorbidity	**Hypertension, ischemic heart disease, myocarditis, ventricular dysplasia, family history of myocardial disease**	**Often no prior cardiac or family history of relevance**
Ejection fraction	**Depressed**	
Frequency of PVCs	**Less than 5000/24 hours**	**More than 10,000/24 hours; often more than 20,000/24 hours**
Pattern of PVCs	**Multi-morphic**	**Monomorphic**
QRS Morphology	**Nonspecific**	**- Outflow tract (right of left bundle-branch block with strong inferior access** **- Fascicular (atypical right bundle-branch block pattern with superior access)**
Response of Temporary Antiarrhythmic Therapy (amiodarone)	**Despite PVCs being suppressed, there is no improvement in myocardial function**	**If PVCs suppressed, myocardial function improves**
Response to Radiofrequency Ablation	**Only required if associated with ventricular tachycardia that has been triggering frequent ICD shocks, no effect on ventricular function**	**Normalization of ventricular function frequently seen**

PVC Burden

- The threshold of ectopy needed to result in TCM has been evaluated by many authors
- There are no clear-cut points that mark the frequency at which cardiomyopathy is unavoidable.
- Niwano et al used a cut point of 20 000 PVCs over 24 hours to define the high-frequency group,
- Kanei et al used a figure of 10 000 PVCs per day.
- Other studies defined "frequent" PVCs as 10% of total beats rather than the absolute number of PVCs,
- Baman et al suggested that a PVC burden of 24% had a sensitivity and specificity of 79% and 78%, respectively, in separating the patient populations with impaired versus preserved LV function

- It is not known why the majority of patients with frequent PVCs have a benign course, whereas up to one third of them develop cardiomyopathy.



Effects of Catheter Ablation of PVCs on Cardiac Function

Taieb et al,[16] 2007	6	Frequent PVCs of various morphologies and LV dysfunction (mean of 17 717 PVCs over 24 h on Holter monitoring)	Successful ablation	Successful ablation in all patients, reduction in PVCs from 17 717±7100 to 268±368 ($P=0.006$)	LVEF increased from 42%±2.5% at baseline to 57%±3% ($P=0.0001$), mean LVEDD decreased from 60.0±3.5 mm to 54.0±3.7 mm ($P=0.0009$)
Sarrazin et al,[19] 2009	30 (15 referred for ablation, 15 served as control)	PVC burden of >5% in patients with prior myocardial infarction	Successful ablation	Successful ablation in all 15 patients, reduction in PVC burden from 22%±12% to 2.6%±5.0%	Significant improvement after ablation in LVEF: mean LVEF increased from 38%±11% to 51%±9% ($P<0.0001$); no improvement in LVEF was noted in the control group
Baman et al,[10] 2010	174 (57 with depressed LVEF 35%±9%)	Frequent PVCs of various morphologies (mean burden of 20%±16% on Holter monitoring)	Successful ablation (80% reduction in PVC burden)	Successful ablation in 146 patients, including 46 of 57 patients with depressed LVEF, reduction in PVC burden from 33%±14% to 1.9%±4.4% ($P<0.01$)	Significant improvement in the 57 patients with depressed LVEF: LVEF increased from 35%±9% at baseline to 54%±10% ($P<0.01$), LVEDD decreased from 59±7 mm to 54±7 mm ($P<0.01$), LVESD decreased from 44±7 mm to 39±8 mm ($P<0.01$)

Recommendations for PVC-Induced Cardiomyopathy

References that support the recommendations are summarized in Online Data Supplement 50.

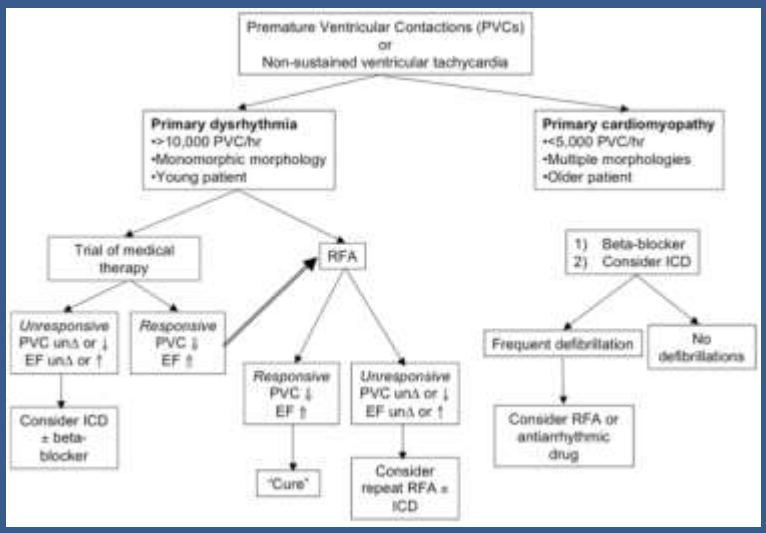
COR	LOE	Recommendations
I	B-NR	1. For patients who require arrhythmia suppression for symptoms or declining ventricular function suspected to be due to frequent PVCs (generally >15% of beats and predominately of 1 morphology) and for whom antiarrhythmic medications are ineffective, not tolerated, or not the patient's preference, catheter ablation is useful (1, 2).
IIa	B-NR	2. In patients with PVC-induced cardiomyopathy, pharmacological treatment (e.g., beta blocker, amiodarone) is reasonable to reduce recurrent arrhythmias and improve symptoms and LV function (3, 4).

PVCs and Exercise

"While some have found that recovery ectopy is more robustly associated with adverse prognosis than exercise ectopy, other results suggest otherwise." ***Dewey*** *F et al (Stanford University Medical School, Palo Alto, CA) report their findings in the January 28, 2008 issue of the Archives of Internal Medicine*

- PVCs that occur during recovery are a stronger predictor of death than PVCs occurring only during exercise (associated with markers of ischemia)
-

Management algorithm for PVCs or NSVT.



Take home message

- PVCs remain a common and vexing problem in cardiology.
- Differentiation between benign & malignant PVCs is an important issue
- RFA is the treatment of choice in the setting of LV dysfunction due to high PVC burden
- Suppression of PVCs is not the aim in the setting of structural heart disease

On PVCs, think anew

but think slowly!!!!!!